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=> d his

     (FILE 'HOME' ENTERED AT 11:03:20 ON 01 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 11:03:48 ON 01 NOV 2007
L1            0 S LOFEPRAMINE (P) L-TYROSINE (P) CYANOCOBALAMIN?

     FILE 'CAPLUS, MEDLINE' ENTERED AT 11:05:16 ON 01 NOV 2007
L2            0 S LOFEPRAMINE (P) L-TYROSINE (P) CYANOCOBALAMIN?
L3            0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L4            0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L5            0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L6            0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L7            0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L8            1 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L9            3 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L10           1 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L11           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) ?
L12           8 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) V
L13           8 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) V
L14          14 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) V
L15           6 S L14 NOT L13
L16           4 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L17           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L18           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L19          26 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L20           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L21           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) L
L22           0 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE)/IT (P
L23           0 S ?DEPRESS?/IT (P) VITAMIN B12/TI
L24           0 S ?DEPRESS/IT (P) VITAMIN B12/TI
L25           0 S DEPRESSANT/IT (P) VITAMIN B12/TI
L26          26 S ?DEPRESS?/TI (P) VITAMIN B12/TI
L27           1 S ?ANTIDEPRESS?/TI (P) VITAMIN B12/TI
L28          25 S DEPRESS?/TI (P) VITAMIN B12/TI

     FILE 'STNGUIDE' ENTERED AT 12:06:06 ON 01 NOV 2007

     FILE 'CAPLUS, MEDLINE' ENTERED AT 12:06:14 ON 01 NOV 2007
L29          14 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) V
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L8 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:417857 CAPLUS
DOCUMENT NUMBER: 125:76407
TITLE: Treatment of multiple sclerosis (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound
INVENTOR(S): Loder, Cari
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611009	A1	19960418	WO 1995-GB2361	19951005
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200761	A1	19960418	CA 1995-2200761	19951005
AU 9536126	A	19960502	AU 1995-36126	19951005
AU 710339	B2	19990916		
GB 2308065	A	19970618	GB 1997-7065	19951005
GB 2308065	B	19990113		
EP 784476	A1	19970723	EP 1995-933488	19951005
EP 784476	B1	20021106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 77380	A2	19980428	HU 1997-2373	19951005
HU 225493	B1	20070129		
JP 10508583	T	19980825	JP 1995-512415	19951005
ZA 9508391	A	19990506	ZA 1995-8391	19951005
SK 281932	B6	20010911	SK 1997-438	19951005
PL 181802	B1	20010928	PL 1995-319830	19951005
AT 227124	T	20021115	AT 1995-933488	19951005
PT 784476	T	20030331	PT 1995-933488	19951005
ES 2184808	T3	20030416	ES 1995-933488	19951005
CZ 293873	B6	20040818	CZ 1997-995	19951005
FI 9701290	A	19970602	FI 1997-1290	19970326
FI 116659	B1	20060131		
NO 9701539	A	19970404	NO 1997-1539	19970404
NO 314486	B1	20030331		
US 6096737	A	20000801	US 1997-817086	19970627
US 6569850	B1	20030527	US 2000-584401	20000601

PRIORITY APPLN. INFO.:	GB 1994-20116	A	19941005
	GB 1995-8482	A	19950426
	WO 1995-GB2361	W	19951005
	US 1997-817086	A3	19970627

AB The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a monoamine oxidase inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of multiple sclerosis or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of 10-220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally

supplemented with injections of vitamin B12. Case histories and composition examples are included.

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS
DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314

PRIORITY APPLN. INFO.: GB 2003-13630 A 20030612
WO 2004-GB2493 W 20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine , tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L9 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:890874 CAPLUS
DOCUMENT NUMBER: 137:362383
TITLE: Treatment of multiple sclerosis with lofepramine, L-phenylalanine and vitamin B12: mechanism of action and clinical importance: roles of the locus coeruleus and central noradrenergic systems
AUTHOR(S): Loder, C.; Allawi, J.; Horrobin, D. F.
CORPORATE SOURCE: Surrey, UK
SOURCE: Medical Hypotheses (2002), 59(5), 594-602
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. In a randomized, placebo-controlled double-blind trial a

combination of lofepramine, phenylalanine and vitamin B12 was found to be effective in relieving the symptoms of multiple sclerosis (MS). The effect occurred within 2-4 wk, and improved all types of symptoms in all types of MS. The combination was also effective in relieving symptoms in patients with chronic pain and chronic fatigue. We hypothesize that the action of this combined therapy may relate to activation of the noradrenergic locus coeruleus/lateral tegmentum (LC/LT) system which has the potential to influence the functioning of large areas of the brain and spinal cord.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:417857 CAPLUS
DOCUMENT NUMBER: 125:76407
TITLE: Treatment of multiple sclerosis (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound
INVENTOR(S): Loder, Cari
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611009	A1	19960418	WO 1995-GB2361	19951005
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200761	A1	19960418	CA 1995-2200761	19951005
AU 9536126	A	19960502	AU 1995-36126	19951005
AU 710339	B2	19990916		
GB 2308065	A	19970618	GB 1997-7065	19951005
GB 2308065	B	19990113		
EP 784476	A1	19970723	EP 1995-933488	19951005
EP 784476	B1	20021106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 77380	A2	19980428	HU 1997-2373	19951005
HU 225493	B1	20070129		
JP 10508583	T	19980825	JP 1995-512415	19951005
ZA 9508391	A	19990506	ZA 1995-8391	19951005
SK 281932	B6	20010911	SK 1997-438	19951005
PL 181802	B1	20010928	PL 1995-319830	19951005
AT 227124	T	20021115	AT 1995-933488	19951005
PT 784476	T	20030331	PT 1995-933488	19951005
ES 2184808	T3	20030416	ES 1995-933488	19951005
CZ 293873	B6	20040818	CZ 1997-995	19951005
FI 9701290	A	19970602	FI 1997-1290	19970326
FI 116659	B1	20060131		
NO 9701539	A	19970404	NO 1997-1539	19970404
NO 314486	B1	20030331		
US 6096737	A	20000801	US 1997-817086	19970627
US 6569850	B1	20030527	US 2000-584401	20000601
PRIORITY APPLN. INFO.:			GB 1994-20116 A	19941005

GB 1995-8482	A	19950426
WO 1995-GB2361	W	19951005
US 1997-817086	A3	19970627

AB The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a monoamine oxidase inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of multiple sclerosis or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of 10-220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally supplemented with injections of vitamin B12 . Case histories and composition examples are included.

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS
DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314
PRIORITY APPLN. INFO.:			GB 2003-13630 A	20030612
			WO 2004-GB2493 W	20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine, tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L12 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:195843 CAPLUS
DOCUMENT NUMBER: 144:343454
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine. [Erratum to document cited in CA144:163994]
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On the Discussion, in the sentence beginning at the bottom of page 526 as "Coppen and Bailey (2000),...", the text "500 mg folic acid or placebo" should read "500 μg folic acid or placebo".

L12 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1066159 CAPLUS
DOCUMENT NUMBER: 144:163994
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 523-528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clin. improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clin. improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (≤2.5 ng/mL) were more likely to experience a later onset of clin. improvement than eufolatemic patients (p=0.0028). B12 and homocysteine level status did not predict time to clin. improvement (p>0.05). In conclusion, low serum folate levels were found to be associated with a delayed onset of clin. improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS

DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314
PRIORITY APPLN. INFO.:			GB 2003-13630 A	20030612
			WO 2004-GB2493 W	20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine, tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L12 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:796266 CAPLUS
DOCUMENT NUMBER: 141:360564
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 2: predictors of relapse during the continuation phase of pharmacotherapy
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Green, Cassandra H.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA
SOURCE: Journal of Clinical Psychiatry (2004), 65(8), 1096-1098
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In the present study, the authors assessed the relationship between serum folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-wk continuation phase of treatment with fluoxetine. Seventy-one outpatients (mean ± SD age = 40.2 ± 11.1 yr; 56.3% women) with MDD (as assessed with the Structured Clin. Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 wk of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of sep. logistic regressions, the authors then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from Nov. 1992 to Jan. 1999. The presence of low serum folate levels ($p = .004$), but not low 13, ($p > .05$) or elevated homocysteine levels ($p > .05$), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% vs. 3.2%, resp. Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:796262 CAPLUS

DOCUMENT NUMBER: 141:360563

TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 1: predictors of clinical response in fluoxetine -resistant depression

AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio

CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA

SOURCE: Journal of Clinical Psychiatry (2004), 65(8), 1090-1095
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study, the authors assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clin. response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-wk, double-blind trial of either (1) fluoxetine dose increase, (2) Li augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine. Fifty-five outpatients (mean ± SD age = 41.7 ± 10.6 yr; 50.9% women) with MDD as assessed with the Structured Clin. Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of a logistic regression, the authors then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clin.

response to double-blind treatment. The study was conducted from Nov. 1992 to Jan. 1999. Low serum folate levels (ηhi2 = 3.626, p = .04), but not elevated homocysteine (p > .05) or low vitamin B12 levels (p > .05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% vs. 44.7%, resp. Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine-resistant MDD.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 6 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2005529418 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15877935
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine.
AUTHOR: Papakostas George I; Petersen Timothy; Lebowitz Barry D; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Alpert Jonathan E; Rosenbaum Jerrold F; Fava Maurizio
CORPORATE SOURCE: Department of Psychiatry, Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: K23-MH069629-1 (NIMH)
R01-MH-48-483-05 (NIMH)
SOURCE: The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum (CINP), (2005 Dec) Vol. 8, No. 4, pp. 523-8. Electronic Publication: 2005-05-09. Journal code: 9815893. ISSN: 1461-1457.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 6 Oct 2005
Last Updated on STN: 6 Jan 2006
Entered Medline: 5 Jan 2006

AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clinical improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clinical improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (<or=2.5 ng/ml) were more likely to experience a later onset of clinical improvement than eufolatemic patients (p =0.0028). B12 and homocysteine level status did not predict time to clinical improvement (p >0.05). In conclusion, low serum folate levels were found to be associated with a delayed onset of clinical improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.

L12 ANSWER 7 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2004454139 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323594
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 1: predictors of clinical response in fluoxetine

-resistant depression.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1090-5.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clinical response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-week, double-blind trial of either (1) fluoxetine dose increase, (2) lithium augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine. METHOD: Fifty-five outpatients (mean +/- SD age = 41.7 +/- 10.6 years; 50.9% women) with MDD as assessed with the Structured Clinical Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of a logistic regression, we then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clinical response to double-blind treatment. The study was conducted from November 1992 to January 1999. RESULTS: Low serum folate levels (chi2=3.626, p =.04), but not elevated homocysteine (p >.05) or low vitamin B12 levels (p >.05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% versus 44.7%, respectively. CONCLUSION: Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine-resistant MDD.

L12 ANSWER 8 OF 8 MEDLINE on STN
ACCESSION NUMBER: 97207503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9054796
TITLE: Folate, vitamin B12, and homocysteine in major depressive disorder.
AUTHOR: Fava M; Borus J S; Alpert J E; Nierenberg A A; Rosenbaum J F; Bottiglieri T
CORPORATE SOURCE: Depression Clinical and Research Program, Clinical Psychopharmacology Unit, Massachusetts General Hospital, Boston 02114, USA.. favam@A1.mgh.harvard.edu
CONTRACT NUMBER: MH-48483 (NIMH)
SOURCE: The American journal of psychiatry, (1997 Mar) Vol. 154, No. 3, pp. 426-8.
Journal code: 0370512. ISSN: 0002-953X.

PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
Entered Medline: 26 Mar 1997

AB OBJECTIVE: The authors examined the relationships between levels of three metabolites (folate, vitamin B12, and homocysteine) and both depressive subtype and response to fluoxetine treatment in depressed patients. METHOD: Fluoxetine, 20 mg/day for 8 weeks, was given to 213 outpatients with major depressive disorder. At baseline, depressive subtypes were assessed, and a blood sample was collected from each patient. Serum metabolite levels were assayed. Response to treatment was determined by percentage change in score on the 17-item Hamilton Depression Rating Scale. RESULTS: Subjects with low folate levels were more likely to have melancholic depression and were significantly less likely to respond to fluoxetine. Homocysteine and B12 levels were not associated with depressive subtype or treatment response. CONCLUSIONS: Overall, the results are consistent with findings linking low folate levels to poorer response to antidepressant treatment. Folate levels might be considered in the evaluation of depressed patients who do not respond to antidepressant treatment.

L15 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:42227 CAPLUS
DOCUMENT NUMBER: 144:329158
TITLE: Brain MRI white matter hyperintensities and one-carbon cycle metabolism in non-geriatric outpatients with major depressive disorder. (Part II)
AUTHOR(S): Papakostas, George I.; Iosifescu, Dan V.; Renshaw, Perry F.; Lyoo, In Kyoon; Lee, Ho Kyu; Alpert, Jonathan E.; Nierenberg, Andrew A.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
SOURCE: Psychiatry Research, Neuroimaging (2005), 140(3), 301-307
CODEN: PSREEK; ISSN: 0925-4927
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of this study was to investigate the relative impact of brain white matter hyperintensities (WMHs), cardiovascular risk factors and elements of the one-carbon cycle metabolism (including serum folate, vitamin B12 and homocysteine levels) on the outcome of antidepressant treatment in non-elderly subjects with major depressive disorder (MDD). Fifty MDD subjects were administered brain magnetic resonance imaging (MRI) scans at 1.5 T to detect T2 WMHs. The severity of brain WMHs was classified with the Fazekas scale (range = 0-3). We assessed cardiovascular risk factors in all MDD subjects (age, gender, smoking, diabetes, family history, hypertension, cholesterol). MDD patients also had serum folate, vitamin B12 and homocysteine levels measured. All MDD subjects received treatment with fluoxetine 20 mg/day for 8 wk. In a logistic regression, the severity of subcortical WMHs and the presence of hypofolatemia were independent predictors of lack of clin. response to antidepressant treatment. Sep., hypofolatemia also predicted lack of remission to antidepressant treatment. These assocns. were independent of the presence of smoking, diabetes, family history, hypercholesterolemia, hyperhomocysteinemia and low B12 levels. Although preliminary, the results of the present work suggest that subcortical brain WMHs and hypofolatemia may have an independent neg. impact on the likelihood of responding to antidepressant treatment in non-geriatric subjects with MDD.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:890874 CAPLUS
DOCUMENT NUMBER: 137:362383
TITLE: Treatment of multiple sclerosis with lofepramine, L-phenylalanine and vitamin B12: mechanism of action and clinical importance: roles of the locus coeruleus and central noradrenergic systems
AUTHOR(S): Loder, C.; Allawi, J.; Horrobin, D. F.
CORPORATE SOURCE: Surrey, UK
SOURCE: Medical Hypotheses (2002), 59(5), 594-602
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. In a randomized, placebo-controlled double-blind trial a combination of lofepramine, phenylalanine and vitamin B12 was found to be effective in relieving the symptoms of multiple sclerosis (MS). The effect occurred within 2-4 wk, and improved all types of symptoms in all types of MS. The combination was also effective in relieving symptoms in

patients with chronic pain and chronic fatigue. We hypothesize that the action of this combined therapy may relate to activation of the noradrenergic locus coeruleus/lateral tegmentum (LC/LT) system which has the potential to influence the functioning of large areas of the brain and spinal cord.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:65830 CAPLUS
DOCUMENT NUMBER: 128:97721
TITLE: Compositions for the treatment of peripheral neuropathies containing antidepressants and/or monoamine oxidase inhibitors and/or vitamin B12 and/or precursors or inducers of a neurotransmitter
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): WWK Trust, UK; Worsley, Andrew Peter
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801157	A1	19980115	WO 1997-GB1822	19970704
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2259010	A1	19980115	CA 1997-2259010	19970704
AU 9734517	A	19980202	AU 1997-34517	19970704
EP 942751	A1	19990922	EP 1997-930634	19970704
EP 942751	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 224733	T	20021015	AT 1997-930634	19970704
PT 942751	T	20030228	PT 1997-930634	19970704
ES 2184111	T3	20030401	ES 1997-930634	19970704
US 2001008884	A1	20010719	US 1999-214314	19990304
US 6335323	B2	20020101		

PRIORITY APPLN. INFO.:	GB 1996-14121	A	19960705
	GB 1996-16019	A	19960731
	WO 1997-GB1822	W	19970704

AB Methods and compns. for treatment of a patient suffering from a form of peripheral neuropathy, e.g. diabetic neuropathy, are disclosed. The method comprises administering to the patient any one of the following combinations of components: (I) A, B and C; (II) A and B; (III) B and C; (IV) A and C; wherein A is an antidepressant or a monoamine oxidase inhibitor, B is vitamin B12, and C is a precursor or inducer of a neurotransmitter, e.g. L-phenylalanine.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:417857 CAPLUS
DOCUMENT NUMBER: 125:76407
TITLE: Treatment of multiple sclerosis (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or

tryptophan and possibly a vitamin B12 compound
INVENTOR(S): Loder, Cari
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611009	A1	19960418	WO 1995-GB2361	19951005
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200761	A1	19960418	CA 1995-2200761	19951005
AU 9536126	A	19960502	AU 1995-36126	19951005
AU 710339	B2	19990916		
GB 2308065	A	19970618	GB 1997-7065	19951005
GB 2308065	B	19990113		
EP 784476	A1	19970723	EP 1995-933488	19951005
EP 784476	B1	20021106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 77380	A2	19980428	HU 1997-2373	19951005
HU 225493	B1	20070129		
JP 10508583	T	19980825	JP 1995-512415	19951005
ZA 9508391	A	19990506	ZA 1995-8391	19951005
SK 281932	B6	20010911	SK 1997-438	19951005
PL 181802	B1	20010928	PL 1995-319830	19951005
AT 227124	T	20021115	AT 1995-933488	19951005
PT 784476	T	20030331	PT 1995-933488	19951005
ES 2184808	T3	20030416	ES 1995-933488	19951005
CZ 293873	B6	20040818	CZ 1997-995	19951005
FI 9701290	A	19970602	FI 1997-1290	19970326
FI 116659	B1	20060131		
NO 9701539	A	19970404	NO 1997-1539	19970404
NO 314486	B1	20030331		
US 6096737	A	20000801	US 1997-817086	19970627
US 6569850	B1	20030527	US 2000-584401	20000601

PRIORITY APPLN. INFO.:	GB 1994-20116	A	19941005
	GB 1995-8482	A	19950426
	WO 1995-GB2361	W	19951005
	US 1997-817086	A3	19970627

AB The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a monoamine oxidase inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of multiple sclerosis or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of 10-220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally supplemented with injections of vitamin B12. Case histories and composition examples are included.

L15 ANSWER 5 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2005623066 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16297603
TITLE: Brain MRI white matter hyperintensities and one-carbon cycle metabolism in non-geriatric outpatients with major

depressive disorder (Part II).
AUTHOR: Papakostas George I; Iosifescu Dan V; Renshaw Perry F; Lyoo In Kyoon; Lee Ho Kyu; Alpert Jonathan E; Nierenberg Andrew A; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.
CONTRACT NUMBER: K23 MH069629 (NIMH)
R01 MH48483 (NIMH)
SOURCE: Psychiatry research, (2005 Dec 30) Vol. 140, No. 3, pp. 301-7. Electronic Publication: 2005-11-16.
Journal code: 7911385. ISSN: 0165-1781.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200602
ENTRY DATE: Entered STN: 24 Nov 2005
Last Updated on STN: 28 Feb 2006
Entered Medline: 24 Feb 2006

AB The objective of this study was to investigate the relative impact of brain white matter hyperintensities (WMHs), cardiovascular risk factors and elements of the one-carbon cycle metabolism (including serum folate, vitamin B12 and homocysteine levels) on the outcome of antidepressant treatment in non-elderly subjects with major depressive disorder (MDD). Fifty MDD subjects were administered brain magnetic resonance imaging (MRI) scans at 1.5 T to detect T2 WMHs. The severity of brain WMHs was classified with the Fazekas scale (range=0-3). We assessed cardiovascular risk factors in all MDD subjects (age, gender, smoking, diabetes, family history, hypertension, cholesterol). MDD patients also had serum folate, vitamin B12 and homocysteine levels measured. All MDD subjects received treatment with fluoxetine 20 mg/day for 8 weeks. In a logistic regression, the severity of subcortical WMHs and the presence of hypofolatemia were independent predictors of lack of clinical response to antidepressant treatment. Separately, hypofolatemia also predicted lack of remission to antidepressant treatment. These associations were independent of the presence of smoking, diabetes, family history, hypercholesterolemia, hyperhomocysteinemia and low B12 levels. Although preliminary, the results of the present work suggest that subcortical brain WMHs and hypofolatemia may have an independent negative impact on the likelihood of responding to antidepressant treatment in non-geriatric subjects with MDD.

L15 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2004454140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323595
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 2: predictors of relapse during the continuation phase of pharmacotherapy.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Green Cassandra H; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1096-8.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-week continuation phase of treatment with fluoxetine. METHOD: Seventy-one outpatients (mean +/- SD age = 40.2 +/- 11.1 years; 56.3% women) with MDD (as assessed with the Structured Clinical Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 weeks of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of separate logistic regressions, we then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from November 1992 to January 1999. RESULTS: The presence of low serum folate levels (p =.004), but not low B12 (p >.05) or elevated homocysteine levels (p >.05), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% versus 3.2%, respectively. CONCLUSION: Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine
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L16 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS
DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314
PRIORITY APPLN. INFO.:			GB 2003-13630 A	20030612
			WO 2004-GB2493 W	20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine, tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L16 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:163459 CAPLUS
DOCUMENT NUMBER: 128:208934
TITLE: Treatment of pain with antidepressants and neurotransmitter inducers/precursors
INVENTOR(S): Horrobin, David Frederick; Cari, Loder; Graham, Cooper
PATENT ASSIGNEE(S): Scotia Holdings PLC, UK
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9808520	A1	19980305	WO 1997-GB2295	19970827
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9740253	A	19980319	AU 1997-40253	19970827
AU 733088	B2	20010503		
EP 1007053	A1	20000614	EP 1997-937721	19970827
EP 1007053	B1	20060628		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
AT 331521	T	20060715	AT 1997-937721	19970827
ES 2264806	T3	20070116	ES 1997-937721	19970827
ZA 9707794	A	19980417	ZA 1997-7794	19970829
US 6451788	B1	20020917	US 2000-242882	20000104
US 2002187958	A1	20021212	US 2002-213905	20020807
US 6989380	B2	20060124		
PRIORITY APPLN. INFO.:			GB 1996-17990 A	19960829
			WO 1997-GB2295 W	19970827
			US 2000-242882 A1	20000104

AB Disclosed is a method of treating pain by the co-administration of an antidepressant together with one or more precursors or inducers of neurotransmitters, particularly amino acids selected from L-phenylalanine, L-tyrosine, L-tryptophan, and L-DOPA. For example, a capsule contained lofepramine 70 and L-phenylalanine 500 mg.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:417857 CAPLUS
DOCUMENT NUMBER: 125:76407
TITLE: Treatment of multiple sclerosis (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound
INVENTOR(S): Loder, Cari
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611009	A1	19960418	WO 1995-GB2361	19951005
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200761	A1	19960418	CA 1995-2200761	19951005
AU 9536126	A	19960502	AU 1995-36126	19951005
AU 710339	B2	19990916		
GB 2308065	A	19970618	GB 1997-7065	19951005
GB 2308065	B	19990113		

EP 784476	A1	19970723	EP 1995-933488	19951005
EP 784476	B1	20021106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 77380	A2	19980428	HU 1997-2373	19951005
HU 225493	B1	20070129		
JP 10508583	T	19980825	JP 1995-512415	19951005
ZA 9508391	A	19990506	ZA 1995-8391	19951005
SK 281932	B6	20010911	SK 1997-438	19951005
PL 181802	B1	20010928	PL 1995-319830	19951005
AT 227124	T	20021115	AT 1995-933488	19951005
PT 784476	T	20030331	PT 1995-933488	19951005
ES 2184808	T3	20030416	ES 1995-933488	19951005
CZ 293873	B6	20040818	CZ 1997-995	19951005
FI 9701290	A	19970602	FI 1997-1290	19970326
FI 116659	B1	20060131		
NO 9701539	A	19970404	NO 1997-1539	19970404
NO 314486	B1	20030331		
US 6096737	A	20000801	US 1997-817086	19970627
US 6569850	B1	20030527	US 2000-584401	20000601
PRIORITY APPLN. INFO.:			GB 1994-20116 A	19941005
			GB 1995-8482 A	19950426
			WO 1995-GB2361 W	19951005
			US 1997-817086 A3	19970627

AB The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a monoamine oxidase inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of multiple sclerosis or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of 10-220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally supplemented with injections of vitamin B12. Case histories and composition examples are included.

L16 ANSWER 4 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2002428756 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12185153
TITLE: A randomised placebo controlled exploratory study of vitamin B-12, lofepramine, and L-phenylalanine (the "Cari Loder regime") in the treatment of multiple sclerosis.
AUTHOR: Wade D T; Young C A; Chaudhuri K R; Davidson D L W
CORPORATE SOURCE: Oxford Centre for Enablement, Oxford, UK.. wade@dial.pipex.com
SOURCE: Journal of neurology, neurosurgery, and psychiatry, (2002 Sep) Vol. 73, No. 3, pp. 246-9.
Journal code: 2985191R. ISSN: 0022-3050.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20 Aug 2002
Last Updated on STN: 25 Sep 2002
Entered Medline: 24 Sep 2002

AB OBJECTIVE: To determine whether combination therapy with lofepramine, L-phenylalanine, and intramuscular vitamin B-12 (the "Cari Loder regime") reduces disability in patients with multiple sclerosis. METHODS: A placebo controlled, double blind, randomised study carried out in five United Kingdom centres on outpatients with clinically definite multiple sclerosis, measurable disability on Guy's neurological disability scale (GNDS), no relapse in

the preceding six months, and not on antidepressant drugs. Over 24 weeks all patients received vitamin B-12, 1 mg intramuscularly weekly, and either lofepramine 70 mg and L-phenylalanine 500 mg twice daily, or matching placebo tablets. Outcome was assessed using the GNDS, the Kurtzke expanded disability status scale; the Beck depression inventory, the Chalder fatigue scale, and the Gulick MS specific symptom scale. RESULTS: 138 patients were entered, and two were lost from each group. There was no statistically significant difference between the groups at entry or at follow up. Analysis of covariance suggested that treated patients had better outcomes on four of the five scales used. Both groups showed a reduction of 2 GNDS points within the first two weeks, and when data from all time points were considered, the treated group had a significant improvement of 0.6 GNDS points from two weeks onwards. CONCLUSIONS: Patients with multiple sclerosis improved by 2 GNDS points after starting vitamin B-12 injections. The addition of lofepramine and L-phenylalanine added a further 0.6 points benefit. More research is needed to confirm and explore the significance of this clinically small difference.

19 ANSWER 16 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2000418095 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10929085
TITLE: Regulation of central corticosteroid receptors following short-term activation of serotonin transmission by 5-hydroxy-L-tryptophan or fluoxetine.
AUTHOR: Semont A; Fache M; Hery F; Faudon M; Youssouf F; Hery M
CORPORATE SOURCE: Laboratoire des Interactions fonctionnelles en Neuroendocrinologie, INSERM U501, Universite de la Mediterranee, IFR Jean-Roche, UER de Medecine Nord, Marseille, France.
SOURCE: Journal of neuroendocrinology, (2000 Aug) Vol. 12, No. 8, pp. 736-44.
Journal code: 8913461. ISSN: 0953-8194.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 15 Sep 2000
Last Updated on STN: 15 Sep 2000
Entered Medline: 6 Sep 2000

AB Alterations of the hypothalamic-pituitary-adrenal (HPA) axis function characterized by a decreased negative feedback capacity are often associated with affective disorders and are corrected by treatment with antidepressant drugs. To gain a better understanding of the effects of the antidepressant drug fluoxetine, a specific serotonin (5-HT) reuptake inhibitor, on central corticosteroid receptors, the effects of short-term activation of serotonin transmission on central corticosteroid receptor expression were analysed in adrenalectomized (ADX) rats either supplemented or not with corticosterone. Serotonin transmission was stimulated either by a single injection of the 5-HT precursor, 5-hydroxy-L-tryptophan (5-HTP), or by a 2-day treatment with fluoxetine. In ADX rats, administration of 5-HTP decreased hippocampal mineralocorticoid (MR) and glucocorticoid (GR) receptor numbers 24 h later, while their respective mRNAs were unchanged and these effects of 5-HTP were mediated by 5-HT2 receptors. In the hypothalamus, GR mRNAs and binding sites decreased 3 h and 24 h after 5-HTP, respectively. By contrast, fluoxetine treatment increased hippocampal MR and GR mRNAs and MR binding sites while GR number remained unchanged. In ADX rats supplemented with corticosterone, 5-HTP and fluoxetine treatment had the same effects on corticosteroid receptors compared to those observed in non supplemented ADX rats: 5-HTP decreased hippocampal MR and GR and hypothalamic GR while fluoxetine treatment increased hippocampal MR. These results show that short-term stimulation of 5-HT transmission by 5-HTP decreases hippocampal and hypothalamic corticosteroid receptor numbers through a corticosterone-independent mechanism. It is hypothesized that the delayed maximal increase in extracellular 5-HT contents after fluoxetine treatment, due to negative feedback regulations induced by the activation of 5-HT1A and 5-HT1B autoreceptors, is not the primary cause for the delayed normalization of corticosteroid receptor numbers that regulates the HPA axis functioning.

L19 ANSWER 17 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2000056317 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10588592
TITLE: Mirtazapine, a mixed-profile serotonin agonist/antagonist, suppresses sleep apnea in the rat.
AUTHOR: Carley D W; Radulovacki M
CORPORATE SOURCE: Department of Medicine, University of Illinois at Chicago, Chicago, Illinois, USA.

CONTRACT NUMBER: AG14564 (NIA)
SOURCE: American journal of respiratory and critical care medicine, (1999 Dec) Vol. 160, No. 6, pp. 1824-9.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 13 Apr 2000
Last Updated on STN: 4 Feb 2003
Entered Medline: 3 Apr 2000

AB Serotonin enhancing drugs, including L-tryptophan and, more recently, fluoxetine and paroxetine, have been tested as pharmacologic treatments for sleep apnea syndrome. Although some patients have demonstrated reduced apnea expression after treatment with these compounds, this improvement has been restricted to nonrapid eye movement (NREM) sleep, with some patients showing no improvement. This study reports the effects of mirtazapine, an antidepressant with 5-HT(1) agonist as well as 5-HT(2) and 5-HT(3) antagonist effects, on sleep and respiration in an established animal model of central apnea. We studied nine adult male Sprague-Dawley rats chronically instrumented for sleep staging. In random order on separate days, rats were recorded after intraperitoneal injection of: (1) saline, (2) 0.1 mg/kg +/- mirtazapine (labeled as Remeron), (3) 1 mg/kg mirtazapine, or (4) 5 mg/ kg mirtazapine. With respect to saline injections, mirtazapine at all three doses reduced apnea index during NREM sleep by more than 50% ($p < 0.0001$) and during REM sleep by 60% ($p < 0.0001$) for at least 6 h. In association with this apnea suppression normalized inspiratory minute ventilation increased during all wake/sleep states ($p < 0.001$ for each state). The duration of NREM sleep was unaffected by any dose of mirtazapine ($p = 0.42$), but NREM EEG delta power was increased by more than 30% at all doses ($p = 0.04$), indicating improved NREM sleep consolidation after mirtazapine injection. We conclude that mirtazapine, over a 50-fold dose range, significantly reduces central apnea expression during NREM and REM sleep in the rat. The efficacy of this compound to suppress apnea in all sleep stages most probably arises from its mixed agonist/antagonist profile at serotonin receptors. The implications of these findings for the management of sleep apnea syndrome must be verified by appropriate clinical trials.

L19 ANSWER 18 OF 26 MEDLINE on STN
ACCESSION NUMBER: 1999457048 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10525755
TITLE: Acute effects of venlafaxine and paroxetine on serotonergic transmission in human volunteers.
AUTHOR: Porter R J; McAllister-Williams R H; Young A H
CORPORATE SOURCE: Department of Neuroscience and Psychiatry, University of Newcastle, Royal Victoria Infirmary, Newcastle NE1 4LP, UK.
SOURCE: Psychopharmacology, (1999 Sep) Vol. 146, No. 2, pp. 194-8.
Journal code: 7608025. ISSN: 0033-3158.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 13 Jan 2000
Last Updated on STN: 13 Jan 2000
Entered Medline: 2 Dec 1999

AB RATIONALE: Antidepressant drugs are thought to enhance

serotonergic neurotransmission through postsynaptic 5-HT(1A) receptors. This effect is delayed in animals and may be paralleled by a delay in the onset of a clinical response in humans. In humans, the growth hormone (GH) response to intravenous l-tryptophan (IV l-TRP) is blocked by the 5-HT(1A) antagonist pindolol and the prolactin response is blunted. Both are therefore thought to be a useful measure of 5-HT(1A) receptor function. Clomipramine has previously been found to enhance the GH and prolactin responses to IV l-TRP after only 2 h. OBJECTIVE: The purpose of this study was to use this method to investigate the effects of newer antidepressants on 5-HT(1A) receptor-mediated function. METHODS: Twelve healthy male volunteers took part in a random order, double blind study, in which 18.75 mg venlafaxine, 5 mg paroxetine or placebo was administered 3 h before infusion of l-TRP. RESULTS: Pretreatment with venlafaxine significantly enhanced the growth hormone (GH) response to the infusion compared with pretreatment with placebo. There was no significant difference between the GH response following paroxetine compared with placebo or with venlafaxine. CONCLUSIONS: The data suggest enhancement of transmission through postsynaptic 5-HT(1A) receptors by venlafaxine but not paroxetine , after only 3 h.

L19 ANSWER 19 OF 26 MEDLINE on STN
ACCESSION NUMBER: 1998322519 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9658383
TITLE: The effect of antidepressants on rat aggressive behavior in the electric footshock and apomorphine-induced aggressiveness paradigms.
AUTHOR: Matto V; Skrebuhhova T; Allikmets L
CORPORATE SOURCE: Department of Pharmacology, University of Tartu, Estonia.. vallo@ut.ee
SOURCE: Methods and findings in experimental and clinical pharmacology, (1998 May) Vol. 20, No. 4, pp. 329-37. Journal code: 7909595. ISSN: 0379-0355.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 6 Oct 1998
Last Updated on STN: 6 Oct 1998
Entered Medline: 18 Sep 1998
AB The effects of acute antidepressant treatment were studied in the electric footshock and apomorphine-induced aggressiveness paradigms and found to be ineffective in both experimental models. In the apomorphine-induced aggressiveness test, 100 mg/kg L-tryptophan challenge manifested the antiaggressive effect of 10 mg/kg fluoxetine (a selective serotonin reuptake inhibitor) treatment. Thus, concomitant L-tryptophan plus fluoxetine treatment decreased the intensity of aggressive postures and increased the time of latency before first attack. In conclusion, our study demonstrates the involvement of the serotoninergic neurotransmission in the neurobiology of aggressive behavior, but after acute treatment in normal rats, the antidepressants do not elicit antiaggressive effects.

L19 ANSWER 20 OF 26 MEDLINE on STN
ACCESSION NUMBER: 95032358 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7945606
TITLE: The serotonin syndrome associated with paroxetine, an over-the-counter cold remedy, and vascular disease.
AUTHOR: Skop B P; Finkelstein J A; Mareth T R; Magoon M R; Brown T M
CORPORATE SOURCE: Department of Psychiatry, Wilford Hall Medical Center,

Lackland Air Force Base, TX 78236-5300.
SOURCE: The American journal of emergency medicine, (1994 Nov) Vol. 12, No. 6, pp. 642-4.
Journal code: 8309942. ISSN: 0735-6757.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199412
ENTRY DATE: Entered STN: 10 Jan 1995
Last Updated on STN: 19 Feb 1996
Entered Medline: 20 Dec 1994

AB There is a new, potentially fatal disorder that is infrequently reported. The apparent rareness may be because of a lack of recognition of the syndrome or its predisposing factors. Fluoxetine (Prozac, Dista Products Co, Division of Eli Lilly Co, Indianapolis, IN), sertraline (Zoloft, Roerig Division, Pfizer Inc, New York, NY), and paroxetine (Paxil, SmithKline Beecham Pharmaceuticals, Philadelphia, PA) belong to a new class of antidepressant medication: the serotonin reuptake-inhibitors (SRIs). The relative safety profile of the SRIs has led to their widespread use. However, a syndrome of excessive serotonergic activity, the "serotonin syndrome" (SS), has recently been recognized. It is characterized by changes in mental status, hypertension, restlessness, myoclonus, hyperreflexia, diaphoresis, shivering, and tremor. A high index of suspicion is required to make the diagnosis in these acutely ill patients. The most common agents implicated in SS are the monoamine oxidase inhibitors in combination with L-tryptophan or fluoxetine. A case of a patient with significant peripheral vascular disease who developed SS while taking paroxetine and an over-the-counter cold medicine is reported. There have been no prior reports of this interaction. Discontinuation of the offending agents, sedation, and supportive care are the mainstays of treatment. The interactions of serotonin with platelets and vascular endothelium are also discussed.

L19 ANSWER 21 OF 26 MEDLINE on STN
ACCESSION NUMBER: 94149169 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8106649
TITLE: Paroxetine: an overview of the efficacy and safety of a new selective serotonin reuptake inhibitor in the treatment of depression.
AUTHOR: Nemeroff C B
CORPORATE SOURCE: Department of Psychiatry and Behavioral Sciences, Emory University School of Medicine, Atlanta, Georgia 30322.
SOURCE: Journal of clinical psychopharmacology, (1993 Dec) Vol. 13, No. 6 Suppl 2, pp. 10S-17S. Ref: 42
Journal code: 8109496. ISSN: 0271-0749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 30 Mar 1994
Last Updated on STN: 30 Mar 1994
Entered Medline: 23 Mar 1994

AB Paroxetine is a novel phenylpiperidine compound that is a potent and selective serotonin reuptake inhibitor. It has little affinity for alpha-adrenergic, dopamine, histamine, and cholinergic receptors. The pharmacokinetic properties of paroxetine are well suited to clinical use. Its bioavailability is not affected by food or antacids; its mean half-life of about 24 hours is consistent with once-a-day dosing;

also, it has no pharmacologically active metabolites. In clinical studies involving over 6,700 patients worldwide, the efficacy of paroxetine has been shown consistently to be superior to placebo and comparable to tricyclic antidepressant agents in the treatment of depression. During these trials, paroxetine was used in a broad range of depressed patients, including the moderately to severely depressed, the elderly, and patients whose depressions were accompanied by symptoms of anxiety. In addition, it has been shown to be effective for the prevention of depressive relapse during long-term treatment. Side effects associated with paroxetine tend to be relatively mild, transient, and easily managed. As with other selective serotonin reuptake inhibitors, the most common side effect associated with paroxetine treatment is nausea, although this effect rarely leads to dose reduction or drug discontinuation. Paroxetine should not be coadministered with monoamine oxidase inhibitors or L-tryptophan. Animal data and limited clinical experience suggest that paroxetine is considerably safer in overdose than are tricyclic antidepressant drugs.

L19 ANSWER 22 OF 26 MEDLINE on STN
ACCESSION NUMBER: 94076381 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8254702
TITLE: Fluoxetine: adverse effects and drug-drug interactions.
AUTHOR: Messiha F S
CORPORATE SOURCE: University of North Dakota School of Medicine, Grand Forks.
SOURCE: Journal of toxicology. Clinical toxicology, (1993) Vol. 31, No. 4, pp. 603-30. Ref: 251
Journal code: 8213460. ISSN: 0731-3810.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199401
ENTRY DATE: Entered STN: 3 Feb 1994
Last Updated on STN: 6 Feb 1998
Entered Medline: 11 Jan 1994

AB This overview summarizes the major and minor side effects and drug interactions of fluoxetine. The adverse reactions include the "serotonin syndrome", cardiovascular complications, extrapyramidal side effects such as akathisia, dyskinesias, and parkinsonian-like syndromes and an apparently increased risk of suicidality. Fluoxetine -induced mania and hypomania, seizures and sexual disorders are evaluated along with minor symptoms of allergic reactions, stuttering, hematological changes, psoriasis, and inappropriate secretion of the antidiuretic hormone. The major fluoxetine-drug interactions involve the amino acids L-dopa and L-tryptophan, anorexiants, anticonvulsants, antidepressants, anxiolytics, calcium channel blockers, cyproheptadine, lithium salts, and drugs of abuse. The underlying mechanism and the paradoxical effects of fluoxetine are addressed.

L19 ANSWER 23 OF 26 MEDLINE on STN
ACCESSION NUMBER: 91328758 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1867646
TITLE: The effects of lofepramine and desmethylimipramine on tryptophan metabolism and disposition in the rat.
AUTHOR: Badawy A A; Morgan C J; Dacey A; Stoppard T
CORPORATE SOURCE: South Glamorgan Health Authority, Biomedical Research Laboratory, Whitchurch Hospital, Cardiff, U.K.
SOURCE: Biochemical pharmacology, (1991 Jul 25) Vol. 42, No. 4, pp. 921-9.
Journal code: 0101032. ISSN: 0006-2952.

PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199109
ENTRY DATE: Entered STN: 29 Sep 1991
Last Updated on STN: 6 Feb 1998
Entered Medline: 9 Sep 1991

AB Acute and chronic administration of lofepramine and its major metabolite desmethylimipramine (DMI) to rats elevates brain tryptophan concentration, thereby enhancing cerebral 5-hydroxytryptamine (5-HT) synthesis, by increasing the availability of circulating tryptophan to the brain, secondarily to inhibition of liver tryptophan pyrrolase (tryptophan 2,3-dioxygenase, L-tryptophan:O2 oxidoreductase, decyclizing; EC 1.13.11.11) activity. The pyrrolase inhibition by lofepramine occurs independently of metabolism to DMI, because it can be demonstrated directly in vitro. Lofepramine also differs from DMI in its action profile on the above and related aspects of tryptophan metabolism and disposition. These results demonstrate that lofepramine influences tryptophan and 5-HT metabolism and disposition independently of its major metabolite DMI, and are discussed briefly in relation to the mechanism of action of antidepressants .

L19 ANSWER 24 OF 26 MEDLINE on STN
ACCESSION NUMBER: 91009054 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2120204
TITLE: New pharmacologic approaches to obsessive compulsive disorder.
AUTHOR: Insel T R
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, Poolesville, Md. 20837.
SOURCE: The Journal of clinical psychiatry, (1990 Oct) Vol. 51 Suppl, pp. 47-51; discussion 56-8. Ref: 36
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 17 Jan 1991
Last Updated on STN: 17 Jan 1991
Entered Medline: 20 Nov 1990

AB Although obsessive compulsive disorder (OCD) traditionally has been considered a treatment-refractory syndrome, rigorous treatment studies over the past decade have demonstrated that most OCD patients respond to specific behavioral or pharmacologic therapies. In terms of the pharmacologic treatment of OCD, a relatively small group of antidepressant drugs (clomipramine, fluvoxamine, and fluoxetine) have been demonstrated to be antiobsessional. Several related antidepressants (desipramine, nortriptyline) appear to be ineffective for OCD. Clinical response requires prolonged treatment (greater than 6 weeks) with antiobsessional drugs and efficacy is not limited to depressed OCD patients. The few drugs that have been demonstrated to be antiobsessional share a high potency for the blockade of serotonin reuptake, suggesting a serotonergic mechanism for antiobsessional drug action. This suggestion has been further strengthened by studies demonstrating a high correlation between clinical response and changes in serotonergic markers with clomipramine treatment. Moreover, a serotonin antagonist, metergoline, appears to partly reverse the improvement observed following chronic clomipramine treatment. Overall, only about 50% of OCD patients appear to respond in any given

pharmacologic treatment trial. Adjunctive treatments, such as lithium or L-tryptophan, have been reported to help in some cases.
In addition, the use of neuroleptics either alone or in combination with antiobsessional drugs may be useful for OCD patients with psychotic features or tics. Pharmacologic treatments should be considered only one element of the therapeutic approach to be integrated with behavioral techniques as well as psychosocial interventions for the relief of this very intriguing syndrome.

L19 ANSWER 25 OF 26 MEDLINE on STN
ACCESSION NUMBER: 90122159 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2692636
TITLE: Obsessive-compulsive disorder as a 5-HT subsystem-related behavioural disorder.
AUTHOR: Murphy D L; Zohar J; Benkelfat C; Pato M T; Pigott T A; Insel T R
CORPORATE SOURCE: Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Maryland.
SOURCE: The British journal of psychiatry. Supplement, (1989 Dec) No. 8, pp. 15-24. Ref: 80
Journal code: 9001294. ISSN: 0960-5371.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199003
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 15 Mar 1990
AB Involvement of the brain serotonin (5-HT) neurotransmitter system in obsessive-compulsive disorder (OCD) was originally suggested on the basis of therapeutic effects found with the semiselective serotonin uptake inhibitor, clomipramine. More recent studies directly comparing clomipramine with non-selective or norepinephrine-selective uptake inhibitors, such as desipramine or nortriptyline, as well as studies with new, more selective serotonin uptake inhibitors, including fluvoxamine and fluoxetine, have supported that hypothesis. Clomipramine's antiobsessional effect has been augmented with the serotonin precursor, L-tryptophan, or with lithium, which has prominent serotonergic effects. Patients whose OCD symptoms improved on clomipramine worsened when the drug was discontinued (regardless of duration of therapy) and improved when clomipramine was reinstituted. OCD symptoms also worsened when metergoline, a 5-HT antagonist, was given to patients who had improved with clomipramine. Metergoline given alone had no effect. Administration of m-chlorophenylpiperazine (m-CPP), a 5-HT receptor agonist, to untreated OCD patients increased their anxiety, depression, and dysphoria, and exacerbated their OC symptoms.
After 4 months of clomipramine therapy, m-CPP failed to produce the same behavioural effects, suggesting an alteration of a 5-HT subsystem (possibly downregulation of some 5-HT receptors). The data reviewed suggest an important role for an abnormal brain 5-HT subsystem in patients with OCD.

L19 ANSWER 26 OF 26 MEDLINE on STN
ACCESSION NUMBER: 84236468 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6734730
TITLE: Behavioral effects of serotonergic and dopaminergic drugs in cats following chronic amphetamine administration.
AUTHOR: Trulson M E; Crisp T
CONTRACT NUMBER: MH 36364 (NIMH)
SOURCE: European journal of pharmacology, (1984 Apr 6) Vol. 99, No. 4, pp. 313-24.
Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198408
ENTRY DATE: Entered STN: 20 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 7 Aug 1984

AB Chronic administration of amphetamine to cats (twice daily, in doses increasing from 5 to 15 mg/kg over a 10-day period) elicited a number of behaviors e.g., limb flicking, abortive grooming, and excessive head shaking, which were originally proposed as an animal behavioral model for studying the actions of hallucinogens that depress central serotonergic neurotransmission. This drug treatment produced large decreases (approximately 50%) in central nervous system serotonin (5HT) and its major metabolite, 5-hydroxyindoleacetic acid, and even larger decreases (approximately 90%) in the levels of dopamine (DA) and norepinephrine. Administration of the 5HT precursors L-tryptophan (25 mg/kg i.p.) or L-5-hydroxytryptophan (12.5 mg/kg i.p.), a direct-acting 5HT agonist (quipazine, 1 mg/kg i.p.) or a monoamine oxidase inhibitor (tranylcypromine, 4 mg/kg i.p.) produced no significant changes in these behaviors in cats treated chronically with amphetamine. Administration of a 5HT reuptake blocker (fluoxetine , 5 mg/kg i.p.) produced a small, but significant, decrease in the frequency of occurrence of these behaviors in amphetamine-treated cats. L-Dihydroxyphenylalanine (L-DOPA, 20 mg/kg i.p.) greatly potentiated these behaviors in cats chronically treated with amphetamine, but L-DOPA was totally ineffective in eliciting these behaviors in naive animals. The behavioral effects of apomorphine (2 mg/kg i.p.) were also significantly potentiated by chronic amphetamine pretreatment. The amino acid precursor of DA, L-tyrosine (25 mg/kg i.p.), and a DA reuptake blocker, bupropion (5 mg/kg i.p.) were without significant effect on these behaviors in amphetamine-treated cats. The data suggest that these cat behaviors are elicited by an action at central DA receptors and that these receptors become supersensitive following chronic amphetamine administration. Furthermore, there may be a qualitative change in DA receptors, since L-DOPA is very effective in potentiating these behaviors in cats treated chronically with amphetamine, but is totally ineffective in naive cats.

L19 ANSWER 6 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:737572 CAPLUS
DOCUMENT NUMBER: 132:30704
TITLE: Acute effects of venlafaxine and paroxetine on serotonergic transmission in human volunteers
AUTHOR(S): Porter, Richard J.; McAllister-Williams, R. Hamish; Young, Allan H.
CORPORATE SOURCE: Department of Neuroscience and Psychiatry, University of Newcastle, Royal Victoria Infirmary, Newcastle, NE1 4LP, UK
SOURCE: Psychopharmacology (Berlin) (1999), 146(2), 194-198
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rationale: Antidepressant drugs are thought to enhance serotonergic neurotransmission through postsynaptic 5-HT1A receptors. This effect is delayed in animals and may be paralleled by a delay in the onset of a clin. response in humans. In humans, the growth hormone (GH) response to i.v. L-tryptophan (IV L-TRP) is blocked by the 5-HT1A antagonist pindolol and the prolactin response is blunted. Both are therefore thought to be a useful measure of 5-HT1A receptor function. Clomipramine has previously been found to enhance the GH and prolactin responses to IV L-TRP after only 2 h. Objective: The purpose of this study was to use this method to investigate the effects of newer antidepressants on 5-HT1A receptor-mediated function. Methods: Twelve healthy male volunteers took part in a random order, double blind study, in which 18.75 mg venlafaxine, 5 mg paroxetine or placebo was administered 3 h before infusion of L-TRP. Results: Pretreatment with venlafaxine significantly enhanced the growth hormone (GH) response to the infusion compared with pretreatment with placebo. There was no significant difference between the GH response following paroxetine compared with placebo or with venlafaxine. Conclusions: The data suggest enhancement of transmission through postsynaptic 5-HT1A receptors by venlafaxine but not paroxetine, after only 3 h.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:106834 CAPLUS
DOCUMENT NUMBER: 130:246901
TITLE: Relationships between low red blood cell count and clinical response to fluoxetine in depressed elderly patients
AUTHOR(S): Mentre, France; Golmard, Jean-Louis; Launay, Jean-Marie; Aubin-Brunet, Valerie; Bouhassira, Myriam; Jouvent, Roland
CORPORATE SOURCE: INSERM U436: Modelisation Mathematique et Statistique en Biologie et, Pitie-Salpetriere Hospital, Paris, 75013, Fr.
SOURCE: Psychiatry Research (1998), 81(3), 403-405
CODEN: PSRSDR; ISSN: 0165-1781
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Biol. variables specifically linked with serotonin deficiency were assessed in geriatric depression. Sixteen depressed patients, all ≥ 60 yr of age and with scores on the Montgomery-Asberg Depression Rating Scale (MADRS) ≥ 20, were treated with fluoxetine (20 mg/day) for 42 days. Biol. variables measured on days 1 and 42 included whole blood and plasma serotonin, plasma total and free tryptophan, and platelet paroxetine and ketanserin binding. Seven of the 16 patients showed a pos.

clin. response (i.e. MADRS score ≤ 12 at day 42). The pre-treatment red blood cell count was the variable most related to clin. response; low levels were found in almost all responders. To a lesser extent, plasma free tryptophan before treatment was also correlated to therapeutic response, with lower values being found in responders. During treatment, plasma free tryptophan was increased in responders and decreased in non-responders. The finding that elderly depressed patients with low pre-treatment red blood cell counts subsequently responded to fluoxetine treatment is consistent with the view that tryptophan, the precursor of serotonin in brain, is taken up by red blood cells.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:434619 CAPLUS
DOCUMENT NUMBER: 129:197872
TITLE: The effect of antidepressants on rat aggressive behavior in the electric footshock and apomorphine-induced aggressiveness paradigms
AUTHOR(S): Matto, Vallo; Skrebuhhova, Tatjana; Allikmets, Lembit
CORPORATE SOURCE: Department of Pharmacology, University of Tartu, Tartu, Estonia
SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1998), 20(4), 329-337
CODEN: MFEPDX; ISSN: 0379-0355
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of acute antidepressant treatment were studied in the elec. footshock and apomorphine-induced aggressiveness paradigms and found to be ineffective in both exptl. models. In the apomorphine-induced aggressiveness test, 100 mg/kg L-tryptophan challenge manifested the antiaggressive effect of 10 mg/kg fluoxetine (a selective serotonin reuptake inhibitor) treatment. Thus, concomitant L-tryptophan plus fluoxetine treatment decreased the intensity of aggressive postures and increased the time of latency before first attack. In conclusion, this study demonstrates the involvement of the serotoninergic neurotransmission in the neurobiol. of aggressive behavior, but after acute treatment in normal rats, the antidepressants do not elicit antiaggressive effects.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:163459 CAPLUS
DOCUMENT NUMBER: 128:208934
TITLE: Treatment of pain with antidepressants and neurotransmitter inducers/precursors
INVENTOR(S): Horrobin, David Frederick; Cari, Loder; Graham, Cooper
PATENT ASSIGNEE(S): Scotia Holdings PLC, UK
SOURCE: PCT Int. Appl., 12 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9808520	A1	19980305	WO 1997-GB2295	19970827

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,

UZ, VN, YU, ZW
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9740253	A	19980319	AU 1997-40253	19970827
AU 733088	B2	20010503		
EP 1007053	A1	20000614	EP 1997-937721	19970827
EP 1007053	B1	20060628		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

AT 331521	T	20060715	AT 1997-937721	19970827
ES 2264806	T3	20070116	ES 1997-937721	19970827
ZA 9707794	A	19980417	ZA 1997-7794	19970829
US 6451788	B1	20020917	US 2000-242882	20000104
US 2002187958	A1	20021212	US 2002-213905	20020807
US 6989380	B2	20060124		

PRIORITY APPLN. INFO.:	GB 1996-17990	A	19960829
	WO 1997-GB2295	W	19970827
	US 2000-242882	A1	20000104

AB Disclosed is a method of treating pain by the co-administration of an antidepressant together with one or more precursors or inducers of neurotransmitters, particularly amino acids selected from L-phenylalanine, L-tyrosine, L-tryptophan, and L-DOPA. For example, a capsule contained lofepramine 70 and L-phenylalanine 500 mg.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 10 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	1997:240609 CAPLUS
DOCUMENT NUMBER:	126:229644
TITLE:	Potentiation of serotonin response
INVENTOR(S):	Wong, David Taiwai
PATENT ASSIGNEE(S):	Eli Lilly and Co., USA
SOURCE:	Eur. Pat. Appl., 29 pp.
	CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 759299	A1	19970226	EP 1996-305999	19960816
EP 759299	B1	20000426		

R: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE

WO 9706792	A1	19970227	WO 1996-US13274	19960816

W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: KE, LS, MW, SD, SZ, UG, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9667761	A	19970312	AU 1996-67761	19960816
AT 192042	T	20000515	AT 1996-305999	19960816
ES 2145977	T3	20000716	ES 1996-305999	19960816
US 5958429	A	19990928	US 1998-11937	19980728
GR 3034007	T3	20001130	GR 2000-401693	20000724

PRIORITY APPLN. INFO.:	US 1995-2440P	P	19950816
	WO 1996-US13274	W	19960816

OTHER SOURCE(S): MARPAT 126:229644

AB The availability of serotonin, norepinephrine, and dopamine in the brain is synergistically increased by administering a serotonin reuptake inhibitor in combination with a serotonin 1A receptor antagonist and L-tryptophan or 5-hydroxy-L-tryptophan for treatment of depression, obsessive-compulsive disorder,

obesity, urinary incontinence, etc. Suitable serotonin reuptake inhibitors include fluoxetine, venlafaxine, citalopram, fluvoxamine, paroxetine, sertraline, milnacipran, and duloxetine. The serotonin 1A receptor antagonist may be e.g. alprenolol, WAY 100135, WAY 100635, spiperone, pindolol, (S)-UH-301, penbutolol, propranolol, or tertatolol. Thus, tablets were prepared containing fluoxetine-HCl 10, (-)-penbutolol 40, 5-hydroxy-L-tryptophan 125, microcryst. cellulose 275, fumed SiO2 10, and stearic acid 5 mg/tablet.

L19 ANSWER 11 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1994:260350 CAPLUS
DOCUMENT NUMBER: 120:260350
TITLE: Fluoxetine: adverse effects and drug-drug interactions
AUTHOR(S): Messiha, F.S.
CORPORATE SOURCE: Sch. Med., Univ. North Dakota, Grand Forks, ND, 58202-9037, USA
SOURCE: Journal of Toxicology, Clinical Toxicology (1993), 31(4), 603-30
CODEN: JTCTDW; ISSN: 0731-3810
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 251 refs. This overview summarizes the major and minor side effects and drug interactions of fluoxetine. The adverse reactions include the "serotonin syndrome", cardiovascular complications, extrapyramidal side effects such as akathisia, dyskinesias, and parkinsonian-like syndromes and an apparently increased risk of suicidality. Fluoxetine-induced mania and hypomania, seizures and sexual disorders are evaluated along with minor symptoms of allergic reactions, stuttering, hematol. changes, psoriasis, and inappropriate secretion of the antidiuretic hormone. The major fluoxetine -drug interactions involve the amino acids L-dopa and L-tryptophan, anorexiants, anticonvulsants, antidepressants , anxiolytics, calcium channel blockers, cyproheptadine, lithium salts, and drugs of abuse. The underlying mechanism and the paradoxical effects of fluoxetine are addressed.

L19 ANSWER 12 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1991:598274 CAPLUS
DOCUMENT NUMBER: 115:198274
TITLE: The effects of lofepramine and demethylimipramine on tryptophan metabolism and disposition in the rat
AUTHOR(S): Badawy, Abdulla A. B.; Morgan, Christopher J.; Dacey, Anthony; Stoppard, Terry
CORPORATE SOURCE: Biomed. Res. Lab., Whitchurch Hosp., Cardiff, CF4 7XB, UK
SOURCE: Biochemical Pharmacology (1991), 42(4), 921-9
CODEN: BCPCA6; ISSN: 0006-2952
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Acute and chronic administration of lofepramine and its major metabolite demethylimipramine (DMI) to rats elevates brain tryptophan concentration, thereby enhancing cerebral 5-hydroxytryptamine (5-HT) synthesis, by increasing the availability of circulating tryptophan to the brain, secondarily to inhibition of liver tryptophan pyrrolase (tryptophan 2,3-dioxygenase, L-tryptophan:O2 oxidoreductase, decyclizing; EC 1.13.11.11) activity. The pyrrolase inhibition by lofepramine occurs independently of metabolism to DMI, because it can be demonstrated directly in vitro. Lofepramine also differs from DMI in its action profile on the above and related aspects of tryptophan metabolism and disposition. These results demonstrate that lofepramine influences tryptophan and 5-HT metabolism and disposition independently of its major metabolite DMI, and are discussed briefly in relation to the mechanism of action of antidepressants.

L19 ANSWER 13 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1984:204150 CAPLUS
DOCUMENT NUMBER: 100:204150
TITLE: Behavioral effects of serotonergic and dopaminergic drugs in cats following chronic amphetamine administration
AUTHOR(S): Trulson, Michael E.; Crisp, Terriann
CORPORATE SOURCE: Lab. Neurobiol., Univ. Texas, Dallas, Richardson, TX, 75080, USA
SOURCE: European Journal of Pharmacology (1984), 99(4), 313-24
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chronic administration of d-amphetamine [51-64-9] to cats (twice daily, in doses increasing from 5 to 15 mg/kg over a 10-day period) elicited a number of behaviors e.g., limb flicking, abortive grooming, and excessive head shaking, which were originally proposed as an animal behavioral model for studying the actions of hallucinogens that depress central serotonergic neurotransmission. This drug treatment produced large decreases (approx. 50%) in central nervous system serotonin (5HT) [50-67-9] and its major metabolite, 5-hydroxyindoleacetic acid [54-16-0], and even larger decreases (approx. 90%) in the levels of dopamine (DA) [51-61-6] and norepinephrine [51-41-2]. Administration of the 5HT precursors L-tryptophan [73-22-3] (25 mg/kg, i.p.) or L-5-hydroxytryptophan [4350-09-8] (12.5 mg/kg, i.p.), a direct-acting 5-HT agonist, quipazine (1 mg/kg, i.p.), or a monoamine oxidase inhibitor, tranylcypromine (4 mg/kg, i.p.) produced no significant changes in these behaviors in cats treated chronically with amphetamine. Administration of a 5HT reuptake blocker, fluoxetine (5 mg/kg, i.p.) produced a small, but significant, decrease in the frequency of occurrence of these behaviors in amphetamine-treated cats. L-Dihydroxyphenylalanine (L-DOPA) [59-92-7] (20 mg/kg, i.p.) greatly potentiated these behaviors in cats chronically treated with amphetamine, but L-DOPA was totally ineffective in eliciting these behaviors in naive animals. The behavioral effects of apomorphine (2 mg/kg, i.p.) were also significantly potentiated by chronic amphetamine pretreatment. The amino acid precursor of DA, L-tyrosine [60-18-4] (25 mg/kg, i.p.), and a DA reuptake blocker, bupropion (5 mg/kg, i.p.) were without significant effect on these behaviors in amphetamine-treated cats. These cat behaviors may be elicited by an action at central DA receptors, and these receptors may become supersensitive following chronic amphetamine administration. Furthermore, there may be a qual. change in DA receptors, since L-DOPA is very effective in potentiating these behaviors in cats treated chronically with amphetamine, but is totally ineffective in naive cats.

L19 ANSWER 14 OF 26 MEDLINE on STN
ACCESSION NUMBER: 2003168763 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12685966
TITLE: Inhibition of tryptophan - pyrrolase activity and elevation of brain tryptophan concentration by fluoxetine in rats.
AUTHOR: Bano Samina; Sherkheli Muhammad Azhar
CORPORATE SOURCE: Department of Biochemistry, University of Karachi, Karachi, Pakistan.
SOURCE: Journal of the College of Physicians and Surgeons--Pakistan : JCPSP, (2003 Jan) Vol. 13, No. 1, pp. 5-10.
Journal code: 9606447. ISSN: 1022-386X.
PUB. COUNTRY: Pakistan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200305
ENTRY DATE: Entered STN: 16 Apr 2003
Last Updated on STN: 2 May 2003

Entered Medline: 1 May 2003

AB OBJECTIVE: To investigate in-vitro as well as in-vivo effects of various doses of fluoxetine (SSRI) on tryptophan metabolism in rats. DESIGN: A pre-clinical study. PLACE AND DURATION OF STUDY: Clinical Biochemistry Research Laboratory, Department of Biochemistry, University of Karachi. The investigation was carried out during 2000 to 2001. SUBJECTS AND METHODS: Male Wistar rats (150-200 g body wt) were selected and divided into control and test groups (n = 5) for comparison. RESULTS: In in-vitro (10 - 1000mM) as well in-vivo (0.5-30 mg/kg body weight) studies, fluoxetine showed a statistically significant inhibition of rat liver tryptophan pyrrolase (tryptophan-2,3-dioxygenase; EC 1.13.11.11) activity. Significant increases were noted at 10 and 30 mg/kg doses in brain, serum (total and free) and liver L-tryptophan concentrations. Similarly, serum non-estrified free fatty acids showed a significant increase at both doses. There was no effect on serum glucose and albumin concentrations. CONCLUSION: It is suggested that major mechanism of action of fluoxetine is that of elevating brain tryptophan concentration and hence 5-HT synthesis by increasing the availability of circulating tryptophan to the brain secondarily to inhibition of major tryptophan degrading enzyme, hepatic tryptophan pyrrolase. It is assumed that fluoxetine inhibits the binding of apoenzyme form of tryptophan pyrrolase with its cofactor haem. The results are discussed in relation to possible involvement of disturbed hepatic tryptophan metabolism in depressive illness.

L19 ANSWER 15 OF 26 MEDLINE on STN

ACCESSION NUMBER: 2002386928 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12130722
TITLE: Effects of antidepressants in rats trained to discriminate centrally administered isoproterenol.
AUTHOR: Crissman Alicia M; O'Donnell James M
CORPORATE SOURCE: Department of Pharmacology, University of Tennessee Health Science Center, 874 Union Avenue, Memphis, TN 38163, USA.. acrissman@utmem.edu
SOURCE: The Journal of pharmacology and experimental therapeutics, (2002 Aug) Vol. 302, No. 2, pp. 606-11. Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200208
ENTRY DATE: Entered STN: 24 Jul 2002
Last Updated on STN: 30 Aug 2002
Entered Medline: 29 Aug 2002

AB Previous work has shown that the discriminative stimulus effects of centrally administered isoproterenol are mediated primarily via beta1-adrenergic receptors. In the present study, this model was used to investigate the ability of antidepressant drugs displaying various pharmacological profiles to stimulate beta1-adrenergic receptors in vivo; this was assessed by determining whether they substituted for the discriminative stimulus effects of isoproterenol. Rats were trained to discriminate centrally administered isoproterenol (10 microg i.c.v.) from artificial cerebral spinal fluid using a water-reinforced, two-lever operant task (fixed ratio 10 schedule). After acquisition of the discrimination, drugs were tested for substitution (i.p.). The tricyclic antidepressants protriptyline and desipramine, the norepinephrine uptake inhibitor nisoxetine, the monoamine oxidase inhibitor phenelzine, and the atypical antidepressants bupropion, mirtazapine, and venlafaxine all produced greater than 90% isoproterenol-appropriate responding. The serotonin uptake inhibitor fluoxetine, the atypical antidepressants buspirone and trazodone, and the novel, putative antidepressants N(G)-nitro-L-arginine and N-acetyl-

L-tryptophan 3,5-bis benzyl ester failed to substitute for isoproterenol at the dose ranges tested. Antagonism studies carried out with betaxolol for those drugs that fully generalized to isoproterenol's cue verified mediation by beta1-adrenergic receptors. The present results indicate that drugs with noradrenergic activity generalize to isoproterenol's discriminative stimulus. Although this suggests a role for central beta1-adrenergic receptors in the mechanism of action of certain antidepressant drugs, it does not seem that stimulation of these receptors is an effect shared by antidepressants from all pharmacological classes.

L19 ANSWER 1 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1087538 CAPLUS
DOCUMENT NUMBER: 146:176894
TITLE: Fluoxetine modulates the circadian biological clock via phase advances of suprachiasmatic nucleus neuronal firing
AUTHOR(S): Sprouse, Jeffrey; Braselton, John; Reynolds, Linda
CORPORATE SOURCE: Department of Neuroscience, Pfizer Global Research and Development, Groton, CT, 06340, USA
SOURCE: Biological Psychiatry (2006), 60(8), 896-899
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: The documented ability of serotonin (5-HT) to directly modulate circadian rhythms prompted interest in a similar role for therapeutic agents that readily enhance 5-HT neurotransmission, namely the selective serotonin reuptake inhibitors (SSRIs). Methods: Extracellular recordings of unit firing of suprachiasmatic nucleus (SCN) neurons maintained in slice culture enabled detns. of circadian rhythmicity. Shifts in the peak of activity were determined during the next circadian cycle following drug exposure. Results: Fluoxetine (10 μm, 60 min incubation) produced robust phase advances only in the presence of L-tryptophan (.5 μm), added to maintain serotonergic tone. Conclusions: Actions of SSRIs at the level of the circadian biol. clock add to the list of pharmacol. effects for this drug class and encourage speculation as to their importance clin.
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 2 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS
DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314
PRIORITY APPLN. INFO.:			GB 2003-13630 A	20030612

WO 2004-GB2493 W 20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine, tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L19 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:567349 CAPLUS
DOCUMENT NUMBER: 138:147554
TITLE: Effects of antidepressants in rats trained to discriminate centrally administered isoproterenol
AUTHOR(S): Crissman, Alicia M.; O'Donnell, James M.
CORPORATE SOURCE: Department of Pharmacology, University of Tennessee Health Science Center, Memphis, TN, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2002), 302(2), 606-611
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous work has shown that the discriminative stimulus effects of centrally administered isoproterenol are mediated primarily via β1-adrenergic receptors. In the present study, this model was used to investigate the ability of antidepressant drugs displaying various pharmacol. profiles to stimulate β1-adrenergic receptors in vivo; this was assessed by determining whether they substituted for the discriminative stimulus effects of isoproterenol. Rats were trained to discriminate centrally administered isoproterenol (10 μg i.c.v.) from artificial cerebral spinal fluid using a water-reinforced, two-lever operant task (fixed ratio 10 schedule). After acquisition of the discrimination, drugs were tested for substitution (i.p.). The tricyclic antidepressants protriptyline and desipramine, the norepinephrine uptake inhibitor nisoxetine, the monoamine oxidase inhibitor phenelzine, and the atypical antidepressants bupropion, mirtazapine, and venlafaxine all produced greater than 90% isoproterenol-appropriate responding. The serotonin uptake inhibitor fluoxetine, the atypical antidepressants buspirone and trazodone, and the novel, putative antidepressants NG-nitro-L-arginine and N-acetyl-L-tryptophan 3,5-bis(trifluoromethyl)benzyl ester failed to substitute for isoproterenol at the dose ranges tested. Antagonism studies carried out with betaxolol for those drugs that fully generalized to isoproterenol's cue verified mediation by β1-adrenergic receptors. The present results indicate that drugs with noradrenergic activity generalize to isoproterenol's discriminative stimulus. Although this suggests a role for central β1-adrenergic receptors in the mechanism of action of certain antidepressant drugs, it does not seem that stimulation of these receptors is an effect shared by antidepressants from all pharmacol. classes.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:548327 CAPLUS
DOCUMENT NUMBER: 133:232693
TITLE: Regulation of central corticosteroid receptors

following short-term activation of serotonin transmission by 5-hydroxy-L-tryptophan or fluoxetine

AUTHOR(S): Semont, A.; Fache, M.-P.; Hery, F.; Faudon, M.; Youssouf, F.; Hery, M.

CORPORATE SOURCE: Laboratoire des Interactions fonctionnelles en Neuroendocrinologie, INSERM U501, Universite de la Mediterranee, IFR Jean-Roche, UER de Medecine Nord, Marseille, 13916, Fr.

SOURCE: Journal of Neuroendocrinology (2000), 12(8), 736-744
CODEN: JOUNE2; ISSN: 0953-8194

PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Alterations of the hypothalamic-pituitary-adrenal (HPA) axis function characterized by a decreased neg. feedback capacity are often associated with affective disorders and are corrected by treatment with antidepressant drugs. To gain a better understanding of the effects of the antidepressant drug fluoxetine, a specific serotonin (5-HT) reuptake inhibitor, on central corticosteroid receptors, the effects of short-term activation of serotonin transmission on central corticosteroid receptor expression were analyzed in adrenalectomized (ADX) rats either supplemented or not with corticosterone. Serotonin transmission was stimulated either by a single injection of the 5-HT precursor, 5-hydroxy-L-tryptophan (5-HTP), or by a 2-day treatment with fluoxetine. In ADX rats, administration of 5-HTP decreased hippocampal mineralocorticoid (MR) and glucocorticoid (GR) receptor nos. 24 h later, while their resp. mRNAs were unchanged and these effects of 5-HTP were mediated by 5-HT2 receptors. In the hypothalamus, GR mRNAs and binding sites decreased 3 h and 24 h after 5-HTP, resp. By contrast, fluoxetine treatment increased hippocampal MR and GR mRNAs and MR binding sites while GR number remained unchanged. In ADX rats supplemented with corticosterone, 5-HTP and fluoxetine treatment had the same effects on corticosteroid receptors compared to those observed in non supplemented ADX rats: 5-HTP decreased hippocampal MR and GR and hypothalamic GR while fluoxetine treatment increased hippocampal MR. These results show that short-term stimulation of 5-HT transmission by 5-HTP decreases hippocampal and hypothalamic corticosteroid receptor nos. through a corticosterone-independent mechanism. It is hypothesized that the delayed maximal increase in extracellular 5-HT contents after fluoxetine treatment, due to neg. feedback regulations induced by the activation of 5-HT1A and 5-HT1B autoreceptors, is not the primary cause for the delayed normalization of corticosteroid receptor nos. that regulates the HPA axis functioning.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L19 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:746539 CAPLUS

DOCUMENT NUMBER: 132:202984

TITLE: Differential changes in brain and platelet 5-HT concentrations after steady-state achievement and repeated administration of antidepressant drugs in mice

AUTHOR(S): Alvarez, J.-C.; Sanceaume, M.; Advenier, C.; Spreux-Varoquaux, O.

CORPORATE SOURCE: Centre Hospitalier de Versailles, Departement de Biochimie-Pharmacologie-Toxicologie, Faculte de Medecine Paris-Ouest-Universite Paris V, Le Chesnay, 78150, Fr.

SOURCE: European Neuropsychopharmacology (1999), 10(1), 31-36
CODEN: EURNE8; ISSN: 0924-977X

PUBLISHER: Elsevier Science Ireland Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of the study was to compare in male NMRI mice the simultaneous evolution of blood serotonin (5-HT) concns., which correspond to 99% of platelet 5-HT content, and 5-HT parameters in the dorsal raphe, caudate nucleus and frontal cortex after clomipramine, fluoxetine and moclobemide treatments. After steady-state concns. of the three compds. were reached, the 5-HT levels were significantly enhanced vs. saline-treated mice in the three brain areas studied. Tryptophan (TRP) levels in the three brain areas were significantly increased with clomipramine and fluoxetine but not with moclobemide. A significant decrease in the metabolite 5-hydroxyindoleacetic acid (5-HIAA) levels was observed only with moclobemide. After 14 days of treatment, 5-HT levels in all areas studied were found to be enhanced only with moclobemide while TRP and 5-HIAA levels were not different under the three drug regimes from those of controls. After 21 days of treatment, 5-HT levels were found enhanced only with moclobemide in the nerve terminal regions. An important depletion in platelet 5-HT content was observed after clomipramine and fluoxetine treatments at day 14 and day 21 and a significant increase was observed after moclobemide treatment at day 14 with a return to initial values after 21 days. Our results show significantly different effects between central and peripheral indexes of 5-HT metabolism according to time and to the antidepressant assessed: (i) an enhancement of total tissue 5-HT levels in the three brain areas studied after steady-state achievement of the 3 antidepressants, (ii) the return to initial values of brain 5-HT levels after repeated administration of the two 5-HT re-uptake inhibitors, consistent with the presence of brain adaptative mechanisms, with a concomitant dramatic decrease of platelet 5-HT content and (iii) an apparent gradual attenuation of the brain and periphery MAOI-A effect induced by moclobemide with 5-HT levels remaining elevated only in 5-HT nerve terminal regions.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:65830 CAPLUS
DOCUMENT NUMBER: 128:97721
TITLE: Compositions for the treatment of peripheral neuropathies containing antidepressants and/or monoamine oxidase inhibitors and/or vitamin B12 and/or precursors or inducers of a neurotransmitter
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): WWK Trust, UK; Worsley, Andrew Peter
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801157	A1	19980115	WO 1997-GB1822	19970704
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2259010	A1	19980115	CA 1997-2259010	19970704
AU 9734517	A	19980202	AU 1997-34517	19970704
EP 942751	A1	19990922	EP 1997-930634	19970704
EP 942751	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 224733	T	20021015	AT 1997-930634	19970704
PT 942751	T	20030228	PT 1997-930634	19970704
ES 2184111	T3	20030401	ES 1997-930634	19970704
US 2001008884	A1	20010719	US 1999-214314	19990304
US 6335323	B2	20020101		

PRIORITY APPLN. INFO.:

GB 1996-14121	A	19960705
GB 1996-16019	A	19960731
WO 1997-GB1822	W	19970704

AB Methods and compns. for treatment of a patient suffering from a form of peripheral neuropathy, e.g. diabetic neuropathy, are disclosed. The method comprises administering to the patient any one of the following combinations of components: (I) A, B and C; (II) A and B; (III) B and C; (IV) A and C; wherein A is an antidepressant or a monoamine oxidase inhibitor, B is vitamin B12, and C is a precursor or inducer of a neurotransmitter, e.g. L-phenylalanine.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 15 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005043957 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15671130
TITLE: Treatment of depression: time to consider folic acid and vitamin B12.
AUTHOR: Coppen Alec; Bolander-Gouaille Christina
CORPORATE SOURCE: MRC Neuropsychiatric Research Laboratory, Epsom, Surrey, UK.. acoppen@globalnet.co.uk
SOURCE: Journal of psychopharmacology (Oxford, England), (2005 Jan) Vol. 19, No. 1, pp. 59-65. Ref: 62
Journal code: 8907828. ISSN: 0269-8811.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 27 Jan 2005
Last Updated on STN: 13 Apr 2005
Entered Medline: 12 Apr 2005

AB We review the findings in major depression of a low plasma and particularly red cell folate, but also of low vitamin B12 status. Both low folate and low vitamin B12 status have been found in studies of depressive patients, and an association between depression and low levels of the two vitamins is found in studies of the general population. Low plasma or serum folate has also been found in patients with recurrent mood disorders treated by lithium. A link between depression and low folate has similarly been found in patients with alcoholism. It is interesting to note that Hong Kong and Taiwan populations with traditional Chinese diets (rich in folate), including patients with major depression, have high serum folate concentrations. However, these countries have very low life time rates of major depression. Low folate levels are furthermore linked to a poor response to antidepressants, and treatment with folic acid is shown to improve response to antidepressants. A recent study also suggests that high vitamin B12 status may be associated with better treatment outcome. Folate and vitamin B12 are major determinants of one-carbon metabolism, in which S-adenosylmethionine (SAM) is formed. SAM donates methyl groups that are crucial for neurological function. Increased plasma homocysteine is a functional marker of both folate and vitamin B12 deficiency. Increased homocysteine levels are found in depressive patients. In a large population study from Norway increased plasma homocysteine was associated with increased risk of depression but not anxiety. There is now substantial evidence of a common decrease in serum/red blood cell folate, serum vitamin B12 and an increase in plasma homocysteine in depression. Furthermore, the MTHFR C677T polymorphism that impairs the homocysteine metabolism is shown to be overrepresented among depressive patients, which strengthens the association. On the basis of current data, we suggest that oral doses of both folic acid (800 microg daily) and vitamin B12 (1 mg daily) should be tried to improve treatment outcome in depression.

L28 ANSWER 16 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004454140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323595
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 2: predictors of relapse during the continuation phase of pharmacotherapy.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Green Cassandra H; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts

General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1096-8.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004
AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-week continuation phase of treatment with fluoxetine. METHOD: Seventy-one outpatients (mean +/- SD age = 40.2 +/- 11.1 years; 56.3% women) with MDD (as assessed with the Structured Clinical Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 weeks of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of separate logistic regressions, we then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from November 1992 to January 1999. RESULTS: The presence of low serum folate levels (p =.004), but not low B12 (p >.05) or elevated homocysteine levels (p >.05), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% versus 3.2%, respectively. CONCLUSION: Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine.

L28 ANSWER 17 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004454139 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323594
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 1: predictors of clinical response in fluoxetine-resistant depression.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1090-5.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)

(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clinical response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-week, double-blind trial of either (1) fluoxetine dose increase, (2) lithium augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine. METHOD: Fifty-five outpatients (mean +/- SD age = 41.7 +/- 10.6 years; 50.9% women) with MDD as assessed with the Structured Clinical Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of a logistic regression, we then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clinical response to double-blind treatment. The study was conducted from November 1992 to January 1999. RESULTS: Low serum folate levels (chi2=3.626, p =.04), but not elevated homocysteine (p >.05) or low vitamin B12 levels (p >.05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% versus 44.7%, respectively. CONCLUSION: Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine-resistant MDD.

L28 ANSWER 18 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2004234056 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14641930
TITLE: High vitamin B12 level and good treatment outcome may be associated in major depressive disorder.
AUTHOR: Hintikka Jukka; Tolmunen Tommi; Tanskanen Antti; Viinamaki Heimo
CORPORATE SOURCE: Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland.. jukka.hintikka@kuh.fi
SOURCE: BMC psychiatry, (2003 Dec 2) Vol. 3, pp. 17. Electronic Publication: 2003-12-02.
Journal code: 100968559. E-ISSN: 1471-244X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 11 May 2004
Last Updated on STN: 7 Jul 2004
Entered Medline: 6 Jul 2004

AB BACKGROUND: Despite of an increasing body of research the associations between vitamin B12 and folate levels and the treatment outcome in depressive disorders are still unsolved. We therefore conducted this naturalistic prospective follow-up study. Our aim was to determine whether there were any associations between the vitamin B12 and folate

level and the six-month treatment outcome in patients with major depressive disorder. Because vitamin B12 and folate deficiency may result in changes in haematological indices, including mean corpuscular volume, red blood cell count and hematocrit, we also examined whether these indices were associated with the treatment outcome. METHODS: Haematological indices, erythrocyte folate and serum vitamin B12 levels were determined in 115 outpatients with DSM-III-R major depressive disorder at baseline and serum vitamin B12 level again on six-month follow-up. The 17-item Hamilton Depression Rating Scale was also compiled, respectively. In the statistical analysis we used chi-squared test, Pearson's correlation coefficient, the Student's t-test, analysis of variance (ANOVA), and univariate and multivariate linear regression analysis. RESULTS: Higher vitamin B12 levels significantly associated with a better outcome. The association between the folate level and treatment outcome was weak and probably not independent. No relationship was found between haematological indices and the six-month outcome. CONCLUSION: The vitamin B12 level and the probability of recovery from major depression may be positively associated. Nevertheless, further studies are suggested to confirm this finding.

L28 ANSWER 19 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003269587 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12796225
TITLE: Folate, vitamin B12, homocysteine, and the MTHFR 677C->T polymorphism in anxiety and depression: the Hordaland Homocysteine Study.
AUTHOR: Bjelland Ingvar; Tell Grethe S; Vollset Stein Emil; Refsum Helga; Ueland Per Magne
CORPORATE SOURCE: Department of Public Health and Primary Health Care, Locus for Homocysteine and Related Vitamins, University of Bergen, Norway.. ingvar.bjelland@uib.no
SOURCE: Archives of general psychiatry, (2003 Jun) Vol. 60, No. 6, pp. 618-26.
Journal code: 0372435. ISSN: 0003-990X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 11 Jun 2003
Last Updated on STN: 15 Jul 2003
Entered Medline: 14 Jul 2003

AB BACKGROUND: An association between depression and folate status has been demonstrated in clinical studies, whereas data are sparse on the relationship between depression and other components of 1-carbon metabolism such as vitamin B12, homocysteine, and the methylenetetrahydrofolate reductase 677C-->T polymorphism. The relationship between anxiety and these components is less well known. This study examined the associations between folate, total homocysteine, vitamin B12, and the methylenetetrahydrofolate reductase 677C-->T polymorphism, and anxiety and depression in a large population-based study. METHODS: Anxiety and depression, measured by the Hospital Anxiety and Depression Scale, were assessed in 5948 subjects aged 46 to 49 years (mean, 47.4 years) and 70 to 74 years (mean, 71.9 years) from the Hordaland Homocysteine Study cohort. By means of logistic regression models, anxiety and depression scores were examined in relation to the factors listed above. RESULTS: Overall, hyperhomocysteinemia (plasma total homocysteine level > or =15.0 micro mol/L [> or =2.02 mg/dL]) (odds ratio, 1.90; 95% confidence interval, 1.11-3.25) and T/T methylenetetrahydrofolate reductase genotype (odds ratio, 1.69; 95% confidence interval, 1.09-2.62), but not low plasma folate or vitamin B12 levels, were significantly related to depression without comorbid anxiety

disorder. Plasma folate level was inversely associated with depression only in the subgroup of middle-aged women. None of the investigated parameters showed a significant relationship to anxiety. CONCLUSION: Our results provide further evidence of a role of impaired 1-carbon metabolism in depression.

L28 ANSWER 20 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2002689666 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12450964
TITLE: Vitamin B12, folate, and homocysteine in depression: the Rotterdam Study.
AUTHOR: Tiemeier Henning; van Tuijl H Ruud; Hofman Albert; Meijer John; Kiliaan Amanda J; Breteler Monique M B
CORPORATE SOURCE: Department of Epidemiology and Biostatistics, Erasmus Medical Centre, PO Box 1738, 3000 DR Rotterdam, The Netherlands.
SOURCE: The American journal of psychiatry, (2002 Dec) Vol. 159, No. 12, pp. 2099-101.
Journal code: 0370512. ISSN: 0002-953X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 14 Dec 2002
Last Updated on STN: 3 Jan 2003
Entered Medline: 2 Jan 2003
AB OBJECTIVE: The associations of vitamin B(12), folate, and homocysteine with depression were examined in a population-based study. METHOD: The authors screened 3,884 elderly people for depressive symptoms. Subjects with positive screening results had psychiatric workups. Folate, vitamin B(12), and homocysteine blood levels were compared in 278 persons with depressive symptoms, including 112 with depressive disorders, and 416 randomly selected reference subjects. Adjustments were made for age, gender, cardiovascular disease, and functional disability. RESULTS: Hyperhomocysteinemia, vitamin B(12) deficiency, and to a lesser extent, folate deficiency were all related to depressive disorders. For folate deficiency and hyperhomocysteinemia, the association with depressive disorders was substantially reduced after adjustment for functional disability and cardiovascular disease, but for vitamin B(12) this appeared independent. CONCLUSIONS: The association of vitamin B(12) and folate with depressive disorders may have different underlying mechanisms. Vitamin B(12) may be causally related to depression, whereas the relation with folate is due to physical comorbidity.

L28 ANSWER 21 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2001120855 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11110989
TITLE: Anemia and macrocytosis in the prediction of serum folate and vitamin B12 status, and treatment outcome in major depression.
AUTHOR: Mischoulon D; Burger J K; Spillmann M K; Worthington J J; Fava M; Alpert J E
CORPORATE SOURCE: Department of Psychiatry, Depression Clinical and Research Program, Massachusetts General Hospital, 15 Parkman St., WAC-812, Boston, MA 02114, USA.. dmischoulon@partners.org
CONTRACT NUMBER: MH-48483 (NIMH)
SOURCE: Journal of psychosomatic research, (2000 Sep) Vol. 49, No. 3, pp. 183-7.
Journal code: 0376333. ISSN: 0022-3999.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 15 Feb 2001

AB BACKGROUND: Folate and B12 deficiencies may result in macrocytic anemia, and are common in major depression; hypofolatemia may result in poorer antidepressant response. We wished to determine whether anemia or macrocytosis predict hypofolatemia, low B12, or refractoriness to antidepressants. METHODS: After obtaining serum folate, B12, and hematological indices, 213 depressed adults were treated with fluoxetine 20 mg/day. Amelioration of depressive symptoms was measured. RESULTS: Neither macrocytosis nor anemia predicted low serum folate/B12, or antidepressant refractoriness. Among 39 patients with hypofolatemia, none had macrocytosis; 28% had low HCT; 41% had low RBC. Among 25 patients with low B12, none had macrocytosis; 24% had low HCT; 28% had low RBC. Among non-responders, 3% had macrocytosis; 24% had low HCT; 25% had low RBC. CONCLUSION: Anemia and macrocytosis should not be used to predict folate or B12 deficiencies, or refractoriness to antidepressants. Measurement of folate and B12 should be considered when evaluating treatment refractoriness.

L28 ANSWER 22 OF 25 MEDLINE on STN
ACCESSION NUMBER: 97207503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9054796
TITLE: Folate, vitamin B12, and homocysteine in major depressive disorder.
AUTHOR: Fava M; Borus J S; Alpert J E; Nierenberg A A; Rosenbaum J F; Bottiglieri T
CORPORATE SOURCE: Depression Clinical and Research Program, Clinical Psychopharmacology Unit, Massachusetts General Hospital, Boston 02114, USA.. favam@A1.mgh.harvard.edu
CONTRACT NUMBER: MH-48483 (NIMH)
SOURCE: The American journal of psychiatry, (1997 Mar) Vol. 154, No. 3, pp. 426-8.
Journal code: 0370512. ISSN: 0002-953X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
Entered Medline: 26 Mar 1997

AB OBJECTIVE: The authors examined the relationships between levels of three metabolites (folate, vitamin B12, and homocysteine) and both depressive subtype and response to fluoxetine treatment in depressed patients. METHOD: Fluoxetine, 20 mg/day for 8 weeks, was given to 213 outpatients with major depressive disorder. At baseline, depressive subtypes were assessed, and a blood sample was collected from each patient. Serum metabolite levels were assayed. Response to treatment was determined by percentage change in score on the 17-item Hamilton Depression Rating Scale. RESULTS: Subjects with low folate levels were more likely to have melancholic depression and were significantly less likely to respond to fluoxetine. Homocysteine and B12 levels were not associated with depressive subtype or treatment response. CONCLUSIONS: Overall, the results are consistent with findings linking low folate levels to poorer response to antidepressant treatment. Folate levels might be considered in the evaluation of depressed patients who do not respond to

antidepressant treatment.

L28 ANSWER 23 OF 25 MEDLINE on STN
ACCESSION NUMBER: 95406341 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7675908
TITLE: [Serum folic acid and vitamin B12 in depressed inpatients. A study of serum folic acid with radioimmunoassay in 121 depressed inpatients].
Serum-Folsaure und Vitamin B12 bei stationaren depressiven Patienten. Untersuchung der Serum-Folsaure mittels Radio-Immuno-Assay bei 121 stationaren Depressiven.
AUTHOR: Wolfersdorf M; Konig F
CORPORATE SOURCE: Abteilung Psychiatrie I der Universitat Ulm, PLK Weissenau, Ravensburg-Weissenau.
SOURCE: Psychiatrische Praxis, (1995 Jul) Vol. 22, No. 4, pp. 162-4.
Journal code: 0423204. ISSN: 0303-4259.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199510
ENTRY DATE: Entered STN: 26 Oct 1995
Last Updated on STN: 26 Oct 1995
Entered Medline: 17 Oct 1995

AB According to the newer literature on folate deficiencies in depressive patients serum folate and vitamin B12 levels were studied (RIA) in 121 consecutively admitted depressive inpatients (47 male, 74 female depressives; age 17-86 years, mean age 48 years, diagnostic by ICD-9 300.4, 296.1) during the first (1-3) days of admission (normal volumes folate 3-17 ng/ml, vitamin B12 200-900 pg/ml). Only in two patients serum folate below 3 ng/ml were found, low vitamin B12 levels (below 200 pg/ml) showed 14 patients. This result is in contrast to other authors who found folate deficiencies in 10-50% of psychiatric patients.

L28 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 91000192 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2206265
TITLE: Relationship of normal serum vitamin B12 and folate levels to cognitive test performance in subtypes of geriatric major depression.
AUTHOR: Bell I R; Edman J S; Miller J; Hebben N; Linn R T; Ray D; Kayne H L
CORPORATE SOURCE: McLean Hospital, Department of Psychiatry (Geriatric Inpatient Service), Belmont, MA 02178.
SOURCE: Journal of geriatric psychiatry and neurology, (1990 Apr-Jun) Vol. 3, No. 2, pp. 98-105.
Journal code: 8805645. ISSN: 0891-9887.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199011
ENTRY DATE: Entered STN: 17 Jan 1991
Last Updated on STN: 6 Feb 1998
Entered Medline: 21 Nov 1990

AB This retrospective study evaluated the relationships between normal serum vitamin B12 and folate levels and neuropsychologic measures in a sample of 60 geriatric inpatients with psychotic depression, nonpsychotic depression, bipolar disorder, and dementia--all consecutively referred for cognitive testing. The psychotic depression subgroup demonstrated

numerous significant positive correlations between B12 and cognitive subtests not seen in other diagnostic subgroups, especially those of IQ, and verbal and visual memory. Metabolic factors including vitamin B12 may play specific roles in the cognitive dysfunctions of different geropsychiatric disorders.

L28 ANSWER 25 OF 25 MEDLINE on STN
ACCESSION NUMBER: 89353209 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3255452
TITLE: Vitamin B12 in psychotic depression.
AUTHOR: Levitt A J; Joffe R T
SOURCE: The British journal of psychiatry : the journal of mental science, (1988 Aug) Vol. 153, pp. 266-7. Journal code: 0342367. ISSN: 0007-1250.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Letter
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198909
ENTRY DATE: Entered STN: 9 Mar 1990
Last Updated on STN: 9 Mar 1990
Entered Medline: 29 Sep 1989

L28 ANSWER 8 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:12902 CAPLUS
DOCUMENT NUMBER: 140:179532
TITLE: High vitamin B12 level and good treatment outcome may be associated in major depressive disorder
AUTHOR(S): Hintikka, Jukka; Tolmunen, Tommi; Tanskanen, Antti; Viinamaki, Heimo
CORPORATE SOURCE: Department of Psychiatry, Kuopio University Hospital, Kuopio, Finland
SOURCE: BMC Psychiatry (2003), 3, No pp. given
CODEN: BPMSCU; ISSN: 1471-244X
URL: http://www.biomedcentral.com/1471-244X/3/17
PUBLISHER: BioMed Central Ltd.
DOCUMENT TYPE: Journal; (online computer file)
LANGUAGE: English
AB Background: Despite of an increasing body of research the assocns. between vitamin B12 and folate levels and the treatment outcome in depressive disorders are still unsolved. We therefore conducted this naturalistic prospective follow-up study. Our aim was to determine whether there were any assocns. between the vitamin B12 and folate level and the six-month treatment outcome in patients with major depressive disorder. Because vitamin B12 and folate deficiency may result in changes in haematol. indexes, including mean corpuscular volume, red blood cell count and hematocrit, we also examined whether these indexes were associated with the treatment outcome. Methods: Haematol. indexes, erythrocyte folate and serum vitamin B12 levels were determined in 115 outpatients with DSM-III-R major depressive disorder at baseline and serum vitamin B12 level again on six-month follow-up. The 17-item Hamilton Depression Rating Scale was also compiled, resp. In the statistical anal. we used chi-squared test, Pearson's correlation coefficient, the Student's t-test, anal. of variance (ANOVA), and univariate and multivariate linear regression anal. Results: Higher vitamin B12 levels significantly associated with a better outcome. The association between the folate level and treatment outcome was weak and probably not independent. No relationship was found between haematol. indexes and the six-month outcome. Conclusion: The vitamin B12 level and the probability of recovery from major depression may be pos. associated Nevertheless, further studies are suggested to confirm this finding.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 9 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:536251 CAPLUS
DOCUMENT NUMBER: 139:147885
TITLE: Folate, vitamin B12, homocysteine, and the MTHFR 677C→T polymorphism in anxiety and depression: the Hordaland Homocysteine Study
AUTHOR(S): Bjelland, Ingvar; Tell, Grethe S.; Vollset, Stein Emil; Refsum, Helga; Ueland, Per Magne
CORPORATE SOURCE: Department of Public Health and Primary Health Care, University of Bergen, Bergen, Norway
SOURCE: Archives of General Psychiatry (2003), 60(6), 618-626
CODEN: ARGPAQ; ISSN: 0003-990X
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: An association between depression and folate status has been demonstrated in clin. studies, whereas data are sparse on the relationship between depression and other components of 1-carbon metabolism such as vitamin B12, homocysteine, and the methylenetetrahydrofolate reductase 677C→T polymorphism. The relationship between anxiety and these components is less well known. This study examined the assocns. between

folate, total homocysteine, vitamin B12, and the methylenetetrahydrofolate reductase 677C→T polymorphism, and anxiety and depression in a large population-based study. Methods: Anxiety and depression, measured by the Hospital Anxiety and Depression Scale, were assessed in 5948 subjects aged 46 to 49 yr (mean, 47.4 yr) and 70 to 74 yr (mean, 71.9 yr) from the Hordaland Homocysteine Study cohort, By means of logistic regression models, anxiety and depression scores were examined in relation to the factors listed above. Results: Overall, hyperhomocysteinemia (plasma total homocysteine level ≥15.0 μmol/L [≥2.02 mg/dL]) (odds ratio, 1.90; 95% confidence interval, 1.11-3.25) and T/T methylenetetrahydrofolate reductase genotype (odds ratio, 1.69; 95% confidence interval, 1.09-2.62), but not low plasma folate or vitamin B12 levels, were significantly related to depression without co-morbid anxiety disorder. Plasma folate level was inversely associated with depression only in the subgroup of middle-aged women. None of the investigated parameters showed a significant relationship to anxiety. Conclusion: Our results provide further evidence of a role of impaired 1-carbon metabolism in depression.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 10 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1973:400402 CAPLUS
DOCUMENT NUMBER: 79:402
TITLE: Depression of the intestinal uptake of radio-vitamin B12 by cholestyramine
AUTHOR(S): Coronato, Andrew; Glass, George B. J.
CORPORATE SOURCE: Dep. Med., New York Med. Coll., New York, NY, USA
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1973), 142(4), 1341-4
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Orally administered cholestyramine [11041-12-6] (4 g) decreased the intestinal absorption of 57Co- and 60Co-labeled vitamin B12 [68-19-9] as measured by the double label hepatic uptake test in normal volunteers and in a patient with pernicious anemia. In the isolated guinea pig intestine it appeared that cholestyramine decreased intrinsic factor-mediated vitamin B12 absorption by binding to a portion of the binding sites on the intrinsic factor mol which normally bind vitamin B12, thereby impairing intrinsic factor-vitamin B12 complex formation.

L28 ANSWER 11 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1959:58201 CAPLUS
DOCUMENT NUMBER: 53:58201
ORIGINAL REFERENCE NO.: 53:10566b-c
TITLE: Comparative tests of the effects of vitamin B12, 5,6-dimethylbenzimidazole, and dibasol on some types of nerve depression
AUTHOR(S): Kolosova, N. N.
SOURCE: Farmakologiya i Toksikologiya (Moscow) (1958), 21(No. 6), 21-4
CODEN: FATOAO; ISSN: 0014-8318
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Dibasol and 5,6-dimethylbenzimidazole, each at 10 mg./kg., and vitamin B12 at 0.0002 mg./kg. alleviate Sechenov's inhibition, spinal shock in frogs, and the nerve effects of pain in mice. Chemical similarities suggest a like mechanism in all 3 cases. Vitamin B12 showed the fastest and dibasol the slowest action.

L28 ANSWER 12 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2007329398 MEDLINE

DOCUMENT NUMBER: PubMed ID: 17320847
TITLE: Correlation of folate, vitamin B12 and homocysteine plasma levels with depression in an elderly Greek population.
AUTHOR: Dimopoulos Nikolaos; Piperi Christina; Salonicioti Aristea; Psarra Vassiliki; Gazi Flerri; Papadimitriou Alexandros; Lea Robert W; Kalofoutis Anastasios
CORPORATE SOURCE: Laboratory of Biological Chemistry, University of Athens Medical School, M. Asias 75, Goudi 11527, Athens, Greece.. dmpnikos@yahoo.gr
SOURCE: Clinical biochemistry, (2007 Jun) Vol. 40, No. 9-10, pp. 604-8. Electronic Publication: 2007-01-26. Journal code: 0133660. ISSN: 0009-9120.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200707
ENTRY DATE: Entered STN: 5 Jun 2007
Last Updated on STN: 24 Jul 2007
Entered Medline: 23 Jul 2007

AB BACKGROUND: Alterations in folate, vitamin B12 and homocysteine plasma levels have been associated with aging, neuronal development and depressive symptomatology. Nevertheless, the associations are not strong enough to suggest the use of these parameters in every day practice for diagnostic or therapeutic purposes. OBJECTIVES: The aim of the study was to investigate the relationship between plasma folate, vitamin B12 and homocysteine in depressive states in the elderly. METHODS: Community-dwelling, elderly individuals over 60 years of age were screened with the Geriatric Depression Scale. The study population was divided into two groups: (a) 33 subjects with depression and (b) 33 healthy controls. All participants were clinically evaluated and completed a questionnaire for socio-demographic and clinical data. Measurements of folate, vitamin B12 and homocysteine were estimated in all blood samples and results were statistically evaluated at $p<0.05$ level of significance. RESULTS: No statistical significance emerged for the socio-demographic data between the two groups. Chronic diseases such as stroke, hypercholesterolemia, hypertension and diabetes also did not differ between the depression and control group. Group (a) had significantly lower levels of folate and vitamin B12 than group (b). Homocysteine was significantly higher in depressed individuals than in controls. CONCLUSION: Lower levels of plasma folate and/or vitamin B12, and higher levels of plasma homocysteine are associated with depression in elderly individuals.

L28 ANSWER 13 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005529418 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15877935
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine.
AUTHOR: Papakostas George I; Petersen Timothy; Lebowitz Barry D; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Alpert Jonathan E; Rosenbaum Jerrold F; Fava Maurizio
CORPORATE SOURCE: Department of Psychiatry, Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: K23-MH069629-1 (NIMH)
R01-MH-48-483-05 (NIMH)
SOURCE: The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum (CINP), (2005 Dec) Vol. 8, No.

4, pp. 523-8. Electronic Publication: 2005-05-09.
Journal code: 9815893. ISSN: 1461-1457.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 6 Oct 2005
Last Updated on STN: 6 Jan 2006
Entered Medline: 5 Jan 2006

AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clinical improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clinical improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (<or=2.5 ng/ml) were more likely to experience a later onset of clinical improvement than eufolatemic patients (p =0.0028). B12 and homocysteine level status did not predict time to clinical improvement (p >0.05). In conclusion, low serum folate levels were found to be associated with a delayed onset of clinical improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.

L28 ANSWER 14 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005222009 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15856723
TITLE: Relationship of homocysteine, folic acid and vitamin B12 with depression in a middle-aged community sample.
AUTHOR: Sachdev Perminder S; Parslow Ruth A; Lux Ora; Salonikas Chris; Wen Wei; Naidoo Daya; Christensen Helen; Jorm Anthony F
CORPORATE SOURCE: School of Psychiatry, University of New South Wales, Sydney, Australia.. p.sachdev@unsw.edu.au
SOURCE: Psychological medicine, (2005 Apr) Vol. 35, No. 4, pp. 529-38.
Journal code: 1254142. ISSN: 0033-2917.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 29 Apr 2005
Last Updated on STN: 24 Aug 2005
Entered Medline: 23 Aug 2005

AB BACKGROUND: Case control studies have supported a relationship between low folic acid and vitamin B112 and high homocysteine levels as possible predictors of depression. The results from epidemiological studies are mixed and largely from elderly populations. METHOD: A random subsample of 412 persons aged 60-64 years from a larger community sample underwent psychiatric and physical assessments, and brain MRI scans. Subjects were assessed using the PRIME-MD Patient Health Questionnaire for syndromal depression and severity of depressive symptoms. Blood measures included serum folic acid, vitamin B12, homocysteine and creatinine levels, and total antioxidant capacity. MRI scans were quantified for brain atrophy, subcortical atrophy, and periventricular and deep white-matter hyperintensity on T2-weighted imaging. RESULTS: Being in the lowest quartile of homocysteine was associated with fewer depressive symptoms,

after adjusting for sex, physical health, smoking, creatinine, folic acid and B12 levels. Being in the lowest quartile of folic acid was associated with increased depressive symptoms, after adjusting for confounding factors, but adjustment for homocysteine reduced the incidence rate ratio for folic acid to a marginal level. Vitamin B12 levels did not have a significant association with depressive symptoms. While white-matter hyperintensities had significant correlations with both homocysteine and depressive symptoms, the brain measures and total antioxidant capacity did not emerge as significant mediating variables. CONCLUSIONS: Low folic acid and high homocysteine, but not low vitamin B12 levels, are correlates of depressive symptoms in community-dwelling middle-aged individuals. The effects of folic acid and homocysteine are overlapping but distinct.

L28 ANSWER 15 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2005043957 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15671130
TITLE: Treatment of depression: time to consider folic acid and vitamin B12.
AUTHOR: Coppen Alec; Bolander-Gouaille Christina
CORPORATE SOURCE: MRC Neuropsychiatric Research Laboratory, Epsom, Surrey, UK.. acoppen@globalnet.co.uk
SOURCE: Journal of psychopharmacology (Oxford, England), (2005 Jan) Vol. 19, No. 1, pp. 59-65. Ref: 62
Journal code: 8907828. ISSN: 0269-8811.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 27 Jan 2005
Last Updated on STN: 13 Apr 2005
Entered Medline: 12 Apr 2005

AB We review the findings in major depression of a low plasma and particularly red cell folate, but also of low vitamin B12 status. Both low folate and low vitamin B12 status have been found in studies of depressive patients, and an association between depression and low levels of the two vitamins is found in studies of the general population. Low plasma or serum folate has also been found in patients with recurrent mood disorders treated by lithium. A link between depression and low folate has similarly been found in patients with alcoholism. It is interesting to note that Hong Kong and Taiwan populations with traditional Chinese diets (rich in folate), including patients with major depression, have high serum folate concentrations. However, these countries have very low life time rates of major depression. Low folate levels are furthermore linked to a poor response to antidepressants, and treatment with folic acid is shown to improve response to antidepressants. A recent study also suggests that high vitamin B12 status may be associated with better treatment outcome. Folate and vitamin B12 are major determinants of one-carbon metabolism, in which S-adenosylmethionine (SAM) is formed. SAM donates methyl groups that are crucial for neurological function. Increased plasma homocysteine is a functional marker of both folate and vitamin B12 deficiency. Increased homocysteine levels are found in depressive patients. In a large population study from Norway increased plasma homocysteine was associated with increased risk of depression but not anxiety. There is now substantial evidence of a common decrease in serum/red blood cell folate, serum vitamin B12 and an increase in plasma homocysteine in depression. Furthermore, the MTHFR C677T polymorphism that impairs the homocysteine metabolism is shown to be overrepresented among depressive patients, which strengthens the association. On the basis of current data, we suggest that oral doses of both folic acid (800 microg daily) and vitamin B12 (1 mg daily) should be tried to improve treatment outcome in depression.

L28 ANSWER 1 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:605821 CAPLUS
TITLE: Correlation of folate, vitamin B12 and homocysteine plasma levels with depression in an elderly Greek population
AUTHOR(S): Dimopoulos, Nikolaos; Piperi, Christina; Salonicioti, Aristea; Psarra, Vassiliki; Gazi, Flerri; Papadimitriou, Alexandros; Lea, Robert W.; Kalofoutis, Anastasios
CORPORATE SOURCE: Laboratory of Biological Chemistry, University of Athens Medical School, Athens, Greece
SOURCE: Clinical Biochemistry (2007), 40(9-10), 604-608
CODEN: CLBIAS; ISSN: 0009-9120
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: Alterations in folate, vitamin B12 and homocysteine plasma levels have been associated with aging, neuronal development and depressive symptomatol. Nevertheless, the assocns. are not strong enough to suggest the use of these parameters in every day practice for diagnostic or therapeutic purposes. Objectives: The aim of the study was to investigate the relationship between plasma folate, vitamin B12 and homocysteine in depressive states in the elderly. Methods: Community-dwelling, elderly individuals over 60 years of age were screened with the Geriatric Depression Scale. The study population was divided into two groups: (a) 33 subjects with depression and (b) 33 healthy controls. All participants were clin. evaluated and completed a questionnaire for socio-demog. and clin. data. Measurements of folate, vitamin B12 and homocysteine were estimated in all blood samples and results were statistically evaluated at $p < 0.05$ level of significance. Results: No statistical significance emerged for the socio-demog. data between the two groups. Chronic diseases such as stroke, hypercholesterolemia, hypertension and diabetes also did not differ between the depression and control group. Group (a) had significantly lower levels of folate and vitamin B12 than group (b). Homocysteine was significantly higher in depressed individuals than in controls. Conclusion: Lower levels of plasma folate and/or vitamin B12, and higher levels of plasma homocysteine are associated with depression in elderly individuals.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 2 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:233609 CAPLUS
DOCUMENT NUMBER: 147:70023
TITLE: Study on serum folic acid and vitamin B12 levels in patients with depression
AUTHOR(S): Zhang, Xinhua; Fan, Chunhong
CORPORATE SOURCE: People's Hospital, Peking University, Beijing, 100044, Peop. Rep. China
SOURCE: Linchuang Jingshen Yixue Zazhi (2006), 16(1), 19-20
CODEN: LJYZA7; ISSN: 1005-3220
PUBLISHER: Linchuang Jingshen Yixue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Serum folic acid and vitamin B12 levels in 76 patients with depression and 67 healthy controls were examined There was not statistically significant differences in mean serum folic acid level and the occurrence of low serum folic acid level between the two groups ($P > 0.05$). The mean serum vitamin B12 level was significantly lower ($P < 0.05$), and the occurrence of low serum vitamin B12 levels was significantly higher in the depression group ($P < 0.01$). In conclusion, depression had some relationship with vitamin B12 deficiency, but no relationship with folic acid.

L28 ANSWER 3 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:195843 CAPLUS
DOCUMENT NUMBER: 144:343454
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine. [Erratum to document cited in CA144:163994]
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On the Discussion, in the sentence beginning at the bottom of page 526 as "Coppen and Bailey (2000),...", the text "500 mg folic acid or placebo" should read "500 μg folic acid or placebo".

L28 ANSWER 4 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1066159 CAPLUS
DOCUMENT NUMBER: 144:163994
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 523-528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clin. improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clin. improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (≤2.5 ng/mL) were more likely to experience a later onset of clin. improvement than eufolatemic patients (p=0.0028). B12 and homocysteine level status did not predict time to clin. improvement (p>0.05). In conclusion, low serum folate levels were found to be associated with a delayed onset of clin. improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:167488 CAPLUS
DOCUMENT NUMBER: 143:25660

TITLE: Treatment of depression: Time to consider folic acid and vitamin B12
AUTHOR(S): Coppen, Alec; Bolander-Gouaille, Christina
CORPORATE SOURCE: MRC Neuropsychiatric Research Laboratory, Epsom, UK
SOURCE: Journal of Psychopharmacology (London, United Kingdom) (2005), 19(1), 59-65
CODEN: JOPSEQ; ISSN: 0269-8811
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. We review the findings in major depression of a low plasma and particularly red cell folate, but also of low vitamin B12 status. Both low folate and low vitamin B12 status have been found in studies of depressive patients, and an association between depression and low levels of the two vitamins is found in studies of the general population. Low plasma or serum folate has also been found in patients with recurrent mood disorders treated by lithium. A link between depression and low folate has similarly been found in patients with alcoholism. It is interesting to note that Hong Kong and Taiwan populations with traditional Chinese diets (rich in folate), including patients with major depression, have high serum folate concns. However, these countries have very low life time rates of major depression. Low folate levels are furthermore linked to a poor response to antidepressants, and treatment with folic acid is shown to improve response to antidepressants. A recent study also suggests that high vitamin B12 status may be associated with better treatment outcome. Folate and vitamin B12 are major determinants of one-carbon metabolism, in which S-adenosylmethionine (SAM) is formed. SAM donates Me groups that are crucial for neurol. function. Increased plasma homocysteine is a functional marker of both folate and vitamin B12 deficiency. Increased homocysteine levels are found in depressive patients. In a large population study from Norway increased plasma homocysteine was associated with increased risk of depression but not anxiety. There is now substantial evidence of a common decrease in serum/red blood cell folate, serum vitamin B12 and an increase in plasma homocysteine in depression. Furthermore, the MTHFR C677T polymorphism that impairs the homocysteine metabolism is shown to be overrepresented among depressive patients, which strengthens the association On the basis of current data, we suggest that oral doses of both folic acid (800 μg daily) and vitamin B12 (1 mg daily) should be tried to improve treatment outcome in depression.
REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:796266 CAPLUS
DOCUMENT NUMBER: 141:360564
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 2: predictors of relapse during the continuation phase of pharmacotherapy
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Green, Cassandra H.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA
SOURCE: Journal of Clinical Psychiatry (2004), 65(8), 1096-1098
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the present study, the authors assessed the relationship between serum

folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-wk continuation phase of treatment with fluoxetine. Seventy-one outpatients (mean ± SD age = 40.2 ± 11.1 yr; 56.3% women) with MDD (as assessed with the Structured Clin. Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 wk of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of sep. logistic regressions, the authors then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from Nov. 1992 to Jan. 1999. The presence of low serum folate levels ($p = .004$), but not low 13, ($p > .05$) or elevated homocysteine levels ($p > .05$), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% vs. 3.2%, resp. Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 7 OF 25 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:796262 CAPLUS

DOCUMENT NUMBER: 141:360563

TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 1: predictors of clinical response in fluoxetine-resistant depression

AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio

CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA

SOURCE: Journal of Clinical Psychiatry (2004), 65(8), 1090-1095
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study, the authors assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clin. response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-wk, double-blind trial of either (1) fluoxetine dose increase, (2) Li augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine. Fifty-five outpatients (mean ± SD age = 41.7 ± 10.6 yr; 50.9% women) with MDD as assessed with the Structured Clin. Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of a logistic regression, the authors then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clin. response to double-blind treatment. The study was conducted from Nov.

1992 to Jan. 1999. Low serum folate levels (ηhi2 = 3.626, p = .04), but not elevated homocysteine (p > .05) or low vitamin B12 levels (p > .05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% vs. 44.7%, resp. Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine-resistant MDD.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 7 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:890874 CAPLUS
DOCUMENT NUMBER: 137:362383
TITLE: Treatment of multiple sclerosis with lofepramine, L-phenylalanine and vitamin B12: mechanism of action and clinical importance: roles of the locus coeruleus and central noradrenergic systems
AUTHOR(S): Loder, C.; Allawi, J.; Horrobin, D. F.
CORPORATE SOURCE: Surrey, UK
SOURCE: Medical Hypotheses (2002), 59(5), 594-602
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. In a randomized, placebo-controlled double-blind trial a combination of lofepramine, phenylalanine and vitamin B12 was found to be effective in relieving the symptoms of multiple sclerosis (MS). The effect occurred within 2-4 wk, and improved all types of symptoms in all types of MS. The combination was also effective in relieving symptoms in patients with chronic pain and chronic fatigue. We hypothesize that the action of this combined therapy may relate to activation of the noradrenergic locus coeruleus/lateral tegmentum (LC/LT) system which has the potential to influence the functioning of large areas of the brain and spinal cord.
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 8 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:65830 CAPLUS
DOCUMENT NUMBER: 128:97721
TITLE: Compositions for the treatment of peripheral neuropathies containing antidepressants and/or monoamine oxidase inhibitors and/or vitamin B12 and/or precursors or inducers of a neurotransmitter
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): WWK Trust, UK; Worsley, Andrew Peter
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9801157	A1	19980115	WO 1997-GB1822	19970704
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2259010	A1	19980115	CA 1997-2259010	19970704
AU 9734517	A	19980202	AU 1997-34517	19970704
EP 942751	A1	19990922	EP 1997-930634	19970704
EP 942751	B1	20020925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
AT 224733	T	20021015	AT 1997-930634	19970704
PT 942751	T	20030228	PT 1997-930634	19970704
ES 2184111	T3	20030401	ES 1997-930634	19970704

US 2001008884	A1	20010719	US 1999-214314		19990304
US 6335323	B2	20020101			
PRIORITY APPLN. INFO.:			GB 1996-14121	A	19960705
			GB 1996-16019	A	19960731
			WO 1997-GB1822	W	19970704

AB Methods and compns. for treatment of a patient suffering from a form of peripheral neuropathy, e.g. diabetic neuropathy, are disclosed. The method comprises administering to the patient any one of the following combinations of components: (I) A, B and C; (II) A and B; (III) B and C; (IV) A and C; wherein A is an antidepressant or a monoamine oxidase inhibitor, B is vitamin B12, and C is a precursor or inducer of a neurotransmitter, e.g. L-phenylalanine.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 9 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1996:417857 CAPLUS
DOCUMENT NUMBER: 125:76407
TITLE: Treatment of multiple sclerosis (MS) and other demyelinating conditions using lofepramine in combination with L-phenylalanine, tyrosine or tryptophan and possibly a vitamin B12 compound
INVENTOR(S): Loder, Cari
PATENT ASSIGNEE(S): UK
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9611009	A1	19960418	WO 1995-GB2361	19951005
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2200761	A1	19960418	CA 1995-2200761	19951005
AU 9536126	A	19960502	AU 1995-36126	19951005
AU 710339	B2	19990916		
GB 2308065	A	19970618	GB 1997-7065	19951005
GB 2308065	B	19990113		
EP 784476	A1	19970723	EP 1995-933488	19951005
EP 784476	B1	20021106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
HU 77380	A2	19980428	HU 1997-2373	19951005
HU 225493	B1	20070129		
JP 10508583	T	19980825	JP 1995-512415	19951005
ZA 9508391	A	19990506	ZA 1995-8391	19951005
SK 281932	B6	20010911	SK 1997-438	19951005
PL 181802	B1	20010928	PL 1995-319830	19951005
AT 227124	T	20021115	AT 1995-933488	19951005
PT 784476	T	20030331	PT 1995-933488	19951005
ES 2184808	T3	20030416	ES 1995-933488	19951005
CZ 293873	B6	20040818	CZ 1997-995	19951005
FI 9701290	A	19970602	FI 1997-1290	19970326
FI 116659	B1	20060131		
NO 9701539	A	19970404	NO 1997-1539	19970404
NO 314486	B1	20030331		

US 6096737	A	20000801	US 1997-817086	19970627
US 6569850	B1	20030527	US 2000-584401	20000601
PRIORITY APPLN. INFO.:			GB 1994-20116	A 19941005
			GB 1995-8482	A 19950426
			WO 1995-GB2361	W 19951005
			US 1997-817086	A3 19970627

AB The use of a combination of a tricyclic or tetracyclic antidepressant, a serotonin reuptake inhibitor, or a monoamine oxidase inhibitor with a neurotransmitter-inducing or precursor compound is proposed in the preparation of medication for the treatment or prevention of multiple sclerosis or other demyelinating conditions. For use in treatment to ameliorate the effects of a demyelinating condition, a daily regime is proposed of 10-220 mg lofepramine and from 100 mg to 5 g of L-phenylalanine, optionally supplemented with injections of vitamin B12. Case histories and composition examples are included.

L29 ANSWER 10 OF 14 MEDLINE on STN

ACCESSION NUMBER:	2005623066 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 16297603
TITLE:	Brain MRI white matter hyperintensities and one-carbon cycle metabolism in non-geriatric outpatients with major depressive disorder (Part II).
AUTHOR:	Papakostas George I; Iosifescu Dan V; Renshaw Perry F; Lyoo In Kyoon; Lee Ho Kyu; Alpert Jonathan E; Nierenberg Andrew A; Fava Maurizio
CORPORATE SOURCE:	Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.
CONTRACT NUMBER:	K23 MH069629 (NIMH) R01 MH48483 (NIMH)
SOURCE:	Psychiatry research, (2005 Dec 30) Vol. 140, No. 3, pp. 301-7. Electronic Publication: 2005-11-16. Journal code: 7911385. ISSN: 0165-1781.
PUB. COUNTRY:	Ireland
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, N.I.H., EXTRAMURAL) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200602
ENTRY DATE:	Entered STN: 24 Nov 2005 Last Updated on STN: 28 Feb 2006 Entered Medline: 24 Feb 2006

AB The objective of this study was to investigate the relative impact of brain white matter hyperintensities (WMHs), cardiovascular risk factors and elements of the one-carbon cycle metabolism (including serum folate, vitamin B12 and homocysteine levels) on the outcome of antidepressant treatment in non-elderly subjects with major depressive disorder (MDD). Fifty MDD subjects were administered brain magnetic resonance imaging (MRI) scans at 1.5 T to detect T2 WMHs. The severity of brain WMHs was classified with the Fazekas scale (range=0-3). We assessed cardiovascular risk factors in all MDD subjects (age, gender, smoking, diabetes, family history, hypertension, cholesterol). MDD patients also had serum folate, vitamin B12 and homocysteine levels measured. All MDD subjects received treatment with fluoxetine 20 mg/day for 8 weeks. In a logistic regression, the severity of subcortical WMHs and the presence of hypofolatemia were independent predictors of lack of clinical response to antidepressant treatment. Separately, hypofolatemia also predicted lack of remission to antidepressant treatment. These associations were independent of the presence of smoking, diabetes, family history, hypercholesterolemia, hyperhomocysteinemia and low B12 levels. Although preliminary, the results of the present work suggest that subcortical brain WMHs and

hypofolatemia may have an independent negative impact on the likelihood of responding to antidepressant treatment in non-geriatric subjects with MDD.

L29 ANSWER 11 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2005529418 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15877935
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine.
AUTHOR: Papakostas George I; Petersen Timothy; Lebowitz Barry D; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Alpert Jonathan E; Rosenbaum Jerrold F; Fava Maurizio
CORPORATE SOURCE: Department of Psychiatry, Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: K23-MH069629-1 (NIMH)
R01-MH-48-483-05 (NIMH)
SOURCE: The international journal of neuropsychopharmacology / official scientific journal of the Collegium Internationale Neuropsychopharmacologicum (CINP), (2005 Dec) Vol. 8, No. 4, pp. 523-8. Electronic Publication: 2005-05-09. Journal code: 9815893. ISSN: 1461-1457.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, N.I.H., EXTRAMURAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 6 Oct 2005
Last Updated on STN: 6 Jan 2006
Entered Medline: 5 Jan 2006

AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clinical improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clinical improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (<or=2.5 ng/ml) were more likely to experience a later onset of clinical improvement than eufolatemic patients (p =0.0028). B12 and homocysteine level status did not predict time to clinical improvement (p >0.05). In conclusion, low serum folate levels were found to be associated with a delayed onset of clinical improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.

L29 ANSWER 12 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004454140 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323595
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 2: predictors of relapse during the continuation phase of pharmacotherapy.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Green Cassandra H; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org

CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1096-8.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-week continuation phase of treatment with fluoxetine. METHOD: Seventy-one outpatients (mean +/- SD age = 40.2 +/- 11.1 years; 56.3% women) with MDD (as assessed with the Structured Clinical Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 weeks of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of separate logistic regressions, we then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from November 1992 to January 1999. RESULTS: The presence of low serum folate levels (p =.004), but not low B12 (p >.05) or elevated homocysteine levels (p >.05), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% versus 3.2%, respectively. CONCLUSION: Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine.

L29 ANSWER 13 OF 14 MEDLINE on STN
ACCESSION NUMBER: 2004454139 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15323594
TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, Part 1: predictors of clinical response in fluoxetine -resistant depression.
AUTHOR: Papakostas George I; Petersen Timothy; Mischoulon David; Ryan Julie L; Nierenberg Andrew A; Bottiglieri Teodoro; Rosenbaum Jerrold F; Alpert Jonathan E; Fava Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA 02114, USA.. gpapakostas@partners.org
CONTRACT NUMBER: 1R01-MH-48-483-05 (NIMH)
SOURCE: The Journal of clinical psychiatry, (2004 Aug) Vol. 65, No. 8, pp. 1090-5.
Journal code: 7801243. ISSN: 0160-6689.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
(COMPARATIVE STUDY)

Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 15 Sep 2004
Last Updated on STN: 22 Sep 2004
Entered Medline: 21 Sep 2004

AB OBJECTIVE: In the present study, we assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clinical response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-week, double-blind trial of either (1) fluoxetine dose increase, (2) lithium augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine . METHOD: Fifty-five outpatients (mean +/- SD age = 41.7 +/- 10.6 years; 50.9% women) with MDD as assessed with the Structured Clinical Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (< or = 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (< or = 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (> or = 13.2 micromol/L) or normal. With the use of a logistic regression, we then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clinical response to double-blind treatment. The study was conducted from November 1992 to January 1999. RESULTS: Low serum folate levels (chi2=3.626, p =.04), but not elevated homocysteine (p >.05) or low vitamin B12 levels (p >.05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% versus 44.7%, respectively. CONCLUSION: Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine-resistant MDD.

L29 ANSWER 14 OF 14 MEDLINE on STN
ACCESSION NUMBER: 97207503 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9054796
TITLE: Folate, vitamin B12, and homocysteine in major depressive disorder.
AUTHOR: Fava M; Borus J S; Alpert J E; Nierenberg A A; Rosenbaum J F; Bottiglieri T
CORPORATE SOURCE: Depression Clinical and Research Program, Clinical Psychopharmacology Unit, Massachusetts General Hospital, Boston 02114, USA.. favam@A1.mgh.harvard.edu
CONTRACT NUMBER: MH-48483 (NIMH)
SOURCE: The American journal of psychiatry, (1997 Mar) Vol. 154, No. 3, pp. 426-8.
Journal code: 0370512. ISSN: 0002-953X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 7 Apr 1997
Last Updated on STN: 7 Apr 1997
Entered Medline: 26 Mar 1997

AB OBJECTIVE: The authors examined the relationships between levels of three metabolites (folate, vitamin B12, and homocysteine)

and both depressive subtype and response to fluoxetine treatment in depressed patients. METHOD: Fluoxetine, 20 mg/day for 8 weeks, was given to 213 outpatients with major depressive disorder. At baseline, depressive subtypes were assessed, and a blood sample was collected from each patient. Serum metabolite levels were assayed. Response to treatment was determined by percentage change in score on the 17-item Hamilton Depression Rating Scale. RESULTS: Subjects with low folate levels were more likely to have melancholic depression and were significantly less likely to respond to fluoxetine. Homocysteine and B12 levels were not associated with depressive subtype or treatment response. CONCLUSIONS: Overall, the results are consistent with findings linking low folate levels to poorer response to antidepressant treatment. Folate levels might be considered in the evaluation of depressed patients who do not respond to antidepressant treatment.

L29 ANSWER 1 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:195843 CAPLUS
DOCUMENT NUMBER: 144:343454
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine. [Erratum to document cited in CA144:163994]
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB On the Discussion, in the sentence beginning at the bottom of page 526 as "Coppen and Bailey (2000),...", the text "500 mg folic acid or placebo" should read "500 μg folic acid or placebo".

L29 ANSWER 2 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:42227 CAPLUS
DOCUMENT NUMBER: 144:329158
TITLE: Brain MRI white matter hyperintensities and one-carbon cycle metabolism in non-geriatric outpatients with major depressive disorder. (Part II)
AUTHOR(S): Papakostas, George I.; Iosifescu, Dan V.; Renshaw, Perry F.; Lyoo, In Kyoon; Lee, Ho Kyu; Alpert, Jonathan E.; Nierenberg, Andrew A.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
SOURCE: Psychiatry Research, Neuroimaging (2005), 140(3), 301-307
CODEN: PSREEK; ISSN: 0925-4927
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of this study was to investigate the relative impact of brain white matter hyperintensities (WMHs), cardiovascular risk factors and elements of the one-carbon cycle metabolism (including serum folate, vitamin B12 and homocysteine levels) on the outcome of antidepressant treatment in non-elderly subjects with major depressive disorder (MDD). Fifty MDD subjects were administered brain magnetic resonance imaging (MRI) scans at 1.5 T to detect T2 WMHs. The severity of brain WMHs was classified with the Fazekas scale (range = 0-3). We assessed cardiovascular risk factors in all MDD subjects (age, gender, smoking, diabetes, family history, hypertension, cholesterol). MDD patients also had serum folate, vitamin B12 and homocysteine levels measured. All MDD subjects received treatment with fluoxetine 20 mg/day for 8 wk. In a logistic regression, the severity of subcortical WMHs and the presence of hypofolatemia were independent predictors of lack of clin. response to antidepressant treatment. Sep., hypofolatemia also predicted lack of remission to antidepressant treatment. These assocns. were independent of the presence of smoking, diabetes, family history, hypercholesterolemia, hyperhomocysteinemia and low B12 levels. Although preliminary, the results of the present work suggest that subcortical brain WMHs and

hypofolatemia may have an independent neg. impact on the likelihood of responding to antidepressant treatment in non-geriatric subjects with MDD.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1066159 CAPLUS
DOCUMENT NUMBER: 144:163994
TITLE: The relationship between serum folate, vitamin B12, and homocysteine levels in major depressive disorder and the timing of improvement with fluoxetine
AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Lebowitz, Barry D.; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Alpert, Jonathan E.; Rosenbaum, Jerrold F.; Fava, Maurizio
CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital Harvard Medical School, Boston, MA, USA
SOURCE: International Journal of Neuropsychopharmacology (2005), 8(4), 523-528
CODEN: IJNUFB; ISSN: 1461-1457
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The objective of the present study was to examine the relationship between serum folate, vitamin B12, and homocysteine levels and the timing of clin. improvement to fluoxetine in major depressive disorder (MDD) patients. A total of 110 outpatients with MDD who responded to an 8-wk trial of fluoxetine had serum folate, B12, and homocysteine measurements at baseline (prior to fluoxetine initiation). Onset of clin. improvement was defined as a 30% decrease in Hamilton Depression Scale scores that led to a 50% decrease by week 8. Patients with low folate levels (≤2.5 ng/mL) were more likely to experience a later onset of clin. improvement than eufolatemic patients ($p=0.0028$). B12 and homocysteine level status did not predict time to clin. improvement ($p>0.05$). In conclusion, low serum folate levels were found to be associated with a delayed onset of clin. improvement during treatment with fluoxetine in MDD by, on average, 1.5 wk.
REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 4 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:1124613 CAPLUS
DOCUMENT NUMBER: 142:49250
TITLE: Compositions for the enhanced treatment of depression
INVENTOR(S): Worsley, Andrew Peter
PATENT ASSIGNEE(S): The WWK Trust, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004110417	A2	20041223	WO 2004-GB2493	20040611
WO 2004110417	A3	20050324		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG

EP 1631276	A2	20060308	EP 2004-736650	20040611
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
US 2007173478	A1	20070726	US 2007-560348	20070314
PRIORITY APPLN. INFO.:			GB 2003-13630	A 20030612
			WO 2004-GB2493	W 20040611

AB For treatment of endogenous depression, there is taken in combination an antidepressant, particularly an selective serotonin reuptake inhibitor (SSRI) or serotonin an noradrenaline reuptake inhibitor (SNRA), and a precursor or inducer of a neurotransmitter, e.g., L-phenylalanine, tyramine or L-tryptophan. Optionally, the patient also takes vitamin B12. For example, a 49 yr old male with chronic endogenous depression was treated with a combination of fluoxetine 30 mg once daily, requiring increasing doses to sustain antidepressant effects, L-phenylalanine 500 mg and vitamin B12 2000 pg orally, all once daily, with a sudden improvement in his depressive condition. He continues to improve clin. on the combination treatment.

L29 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2004:796266 CAPLUS
DOCUMENT NUMBER:	141:360564
TITLE:	Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 2: predictors of relapse during the continuation phase of pharmacotherapy
AUTHOR(S):	Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Green, Cassandra H.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio
CORPORATE SOURCE:	Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA
SOURCE:	Journal of Clinical Psychiatry (2004), 65(8), 1096-1098 CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER:	Physicians Postgraduate Press, Inc.
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB In the present study, the authors assessed the relationship between serum folate, vitamin B12, and homocysteine levels on the rate of relapse in outpatients with remitted major depressive disorder (MDD) during a 28-wk continuation phase of treatment with fluoxetine. Seventy-one outpatients (mean ± SD age = 40.2 ± 11.1 yr; 56.3% women) with MDD (as assessed with the Structured Clin. Interview for DSM-III-R) who had remitted and who were enrolled in the continuation phase of treatment with fluoxetine had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to acute-phase treatment). Patients were followed for 28 wk of continued treatment with fluoxetine 40 mg/day to monitor for depressive relapse. Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of sep. logistic regressions, the authors then assessed the relationship between folate, vitamin B12, and homocysteine level status and relapse. The study was conducted from Nov. 1992 to Jan. 1999. The presence of low serum folate levels (p = .004), but not low 13, (p > .05) or elevated homocysteine

levels (p > .05), was associated with relapse during continuation treatment with fluoxetine. The relapse rates for patients with (N = 7) and without (N = 64) low folate levels were 42.9% vs. 3.2%, resp. Low serum folate levels were found to place patients with remitted MDD at risk for depressive relapse during the continuation phase of treatment with fluoxetine.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 14 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:796262 CAPLUS

DOCUMENT NUMBER: 141:360563

TITLE: Serum folate, vitamin B12, and homocysteine in major depressive disorder, part 1: predictors of clinical response in fluoxetine -resistant depression

AUTHOR(S): Papakostas, George I.; Petersen, Timothy; Mischoulon, David; Ryan, Julie L.; Nierenberg, Andrew A.; Bottiglieri, Teodoro; Rosenbaum, Jerrold F.; Alpert, Jonathan E.; Fava, Maurizio

CORPORATE SOURCE: Depression Clinical and Research Program, Massachusetts General Hospital, Harvard Medical School, Boston, USA

SOURCE: Journal of Clinical Psychiatry (2004), 65(8), 1090-1095
CODEN: JCLPDE; ISSN: 0160-6689

PUBLISHER: Physicians Postgraduate Press, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In the present study, the authors assessed the relationship between serum folate, vitamin B12, and homocysteine levels and clin. response in patients with major depressive disorder (MDD) who had previously failed to respond to open treatment with fluoxetine 20 mg/day and were enrolled in a 4-wk, double-blind trial of either (1) fluoxetine dose increase, (2) Li augmentation of fluoxetine, or (3) desipramine augmentation of fluoxetine. Fifty-five outpatients (mean ± SD age = 41.7 ± 10.6 yr; 50.9% women) with MDD as assessed with the Structured Clin. Interview for DSM-III-R who were enrolled in the double-blind trial had serum folate, vitamin B12, and homocysteine measurements completed at baseline (prior to fluoxetine treatment initiation). Folate levels were classified as either low (≤ 2.5 ng/mL) or normal. Vitamin B12 levels were classified as either low (≤ 200 pg/mL) or normal. Homocysteine levels were classified as either elevated (≥ 13.2 μmol/L) or normal. With the use of a logistic regression, the authors then assessed the relationship between (1) low or normal folate levels, (2) normal or low B12 levels, and (3) elevated or normal homocysteine levels and clin. response to double-blind treatment. The study was conducted from Nov. 1992 to Jan. 1999. Low serum folate levels (ηhi2 = 3.626, p = .04), but not elevated homocysteine (p > .05) or low vitamin B12 levels (p > .05), were associated with poorer response to treatment. The response rates for patients with (N = 14) and without (N = 38) low folate levels were 7.1% vs. 44.7%, resp. Low serum folate levels were found to be associated with further treatment resistance among patients with fluoxetine -resistant MDD.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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     (FILE 'HOME' ENTERED AT 11:03:20 ON 01 NOV 2007)

     FILE 'REGISTRY' ENTERED AT 11:03:48 ON 01 NOV 2007
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     FILE 'CAPLUS, MEDLINE' ENTERED AT 11:05:16 ON 01 NOV 2007
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     FILE 'CAPLUS, MEDLINE' ENTERED AT 12:06:14 ON 01 NOV 2007
L29          14 S (LOFEPRAMINE OR FLUOXETINE OR CITALAPRAM OR PAROXETINE) (P) V
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